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THE AMERICAN HEART JOURNAL

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The American Heart Journal

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The American Heart Journal

VOL. 10 FEBRUARY, 1935 No. 3

Original Communications

LOCALIZATION OF CARDIAC INFARCTS ACCORDING TO COMPONENT VENTRICULAR MUSCLES*†

JANE SANDS ROBB, M.D., J. G. FRED HISS, M.D., AND
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ON REVIEWING the literature of the past fifteen years one is impressed by the number of attempts to correlate the electrocardiographic findings with the anatomical lesions found in cases of coronary thrombosis. We are probably not minimizing the truth when we say that success has not been great. All these attempts at localization have been made either in terms of topography of the heart, e.g., right or left ventricle, anterior or posterior surface, base or apex, etc., or in terms of the larger branches of the coronary arteries, as the descending or circumflex branch of the left coronary, etc.

We have approached the problem from a different angle, using the individual ventricular muscles as a basis. There have been many attempts to divide the heart muscle into its component bundles, the most noteworthy being those by MacCallum,[1] Mall,[2] and Tandler.[3] Robb[4] has recently repeated this work and is adding to it a study of the coronary supply to each muscle band. She noted that many of the smaller vessels supplied only one or predominantly one of these muscle bundles, in this respect resembling the end arteries to skeletal muscle. In subsequent experiments advantage was taken of this one-muscle distribution to produce a localized ischemia by ligating these end arteries in 21 dogs. The immediate effects upon the electrocardiogram and on the blood pressure

*From the Departments of Pharmacology and Medicine, College of Medicine, Syracuse University.

Read at the Tenth Scientific Session of the American Heart Association. Cleveland, June 12, 1934.

†This work was supported by a grant from the Committee on Scientific Research of the American Medical Association, and also by the Hendricks Research Fund of Syracuse University.

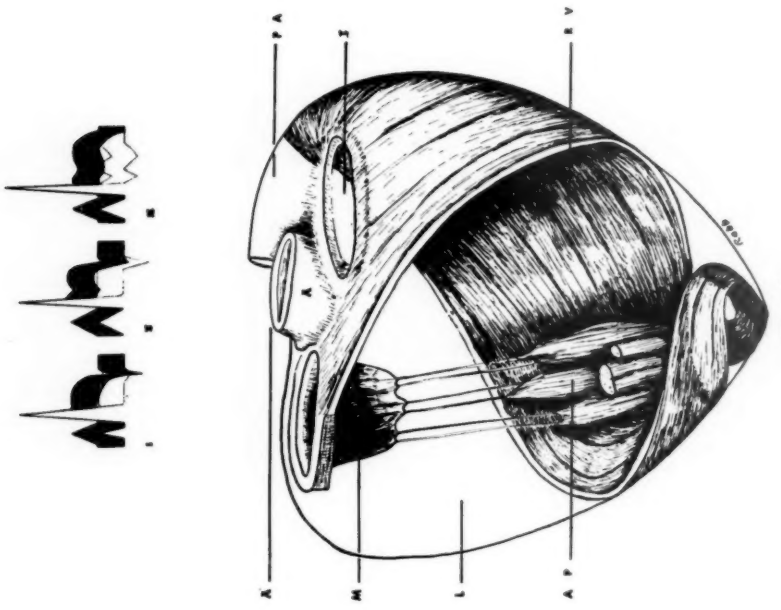

Fig. 2.

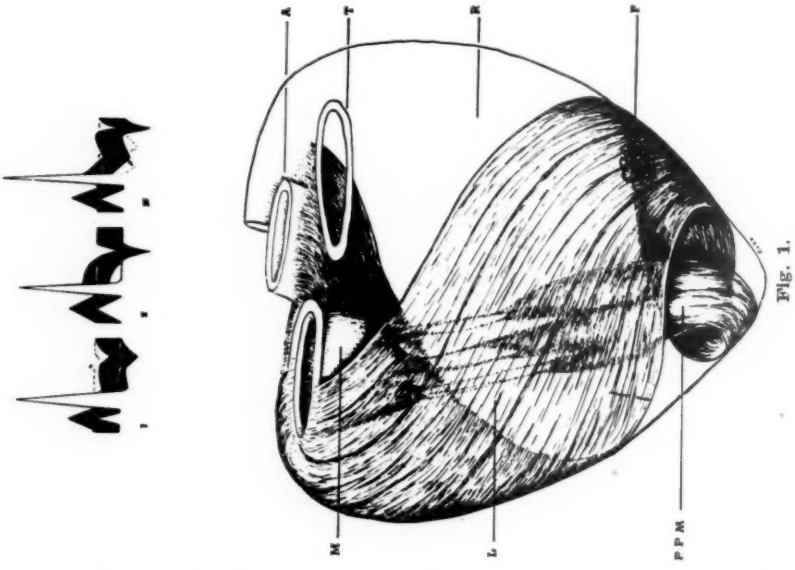

Fig. 1.

Fig. 1.—Superficial bulbospiral muscle, posterior view. Origin from portions of the left A-V ring. Insertion, mainly through the posterior papillary muscle and the posterior leaflet of the mitral valve to the left A-V ring. Certain of the branches of the anterior and posterior descending coronary arteries are "end arteries" to the internal portion of this muscle. The characteristic electrocardiogram for injury to this muscle shows depression of R-T in Lead I and elevation of R-T in Leads II and III.*

Fig. 2.—Superficial sinospiral muscle, posterior view. Origin mainly from the right A-V ring. Insertion, mainly through the anterior papillary and anterior leaflet of the mitral valve to the left A-V ring. Branches of the anterior descending coronary artery are "end arteries" to the internal portion of this muscle. The characteristic electrocardiogram for injury to this muscle shows slight elevation of R-T. in all leads.

were noted. Four of the six ventricular muscles are available for such a study, e.g., the superficial sinospiral, superficial bulbospiral, deep sinospiral, deep bulbospiral.

As a complete control for each ligation, after the heart had been removed, the ligated vessel was injected with a dye, just distal to the ligature. The heart was then dissected so that it could be established that in a particular case the blood vessel in question did supply only the one muscle and that the resulting electrocardiogram was due to injury of that muscle alone.

Four types of muscle injury have been studied: (1) ischemia, (2) compression, (3) cutting, (4) injury to the internal attachment of the muscle (probably injury to the Purkinje material) by an instrument inserted through the auricular appendage and passed down into the ventricle. Regardless of the type of injury the electrocardiographic changes are consistent for each muscle. A few attempts were made to use freezing as a method of injury, but were discarded since it was not possible to localize the temperature change to one muscle.

Blood pressure was recorded through a carotid cannula and a mercury manometer. Injury to the superficial muscles caused little fall in blood pressure, usually less than 5 mm. of mercury. Injury to either of the deep muscles caused a fall in blood pressure, equal to 20 per cent to 50 per cent of the original value. If several vessels were ligated in rapid succession, death was immediate.

The details of the findings are presented in Figs. 1-4 and their legends. Because of limited facilities it was not possible to carry on chronic experiments, hence it must be emphasized that the results given are for acute experiments lasting up to ten hours.

DISCUSSION

Fortunately some experiments by other investigators are so well reported and illustrated (especially those of Fred Smith and his coworkers[5]) that we do have some idea of the after effects of lesions of individual muscles. It is interesting to note that both Smith,[5] and Barnes and Mann[6] obtained electrocardiograms similar to ours when the only manipulation consisted in opening the pericardium. Both investigators state, however, that at autopsy there was in each case a definite acute myocarditis involving the superficial muscle fibers, thus illustrating another method of muscle injury which causes the same characteristic changes in the electrocardiogram.

---

*In each illustration, I, II, and III indicate the corresponding leads. The dotted lines indicate the normal control.

A, aorta; *A P*, anterior papillary muscle; *L*, left ventricle; *M*, mitral valve; *O*, origin of deep sinospiral muscle; *P*, fibers to the right anterior papillary; *P A*, pulmonary artery; *P P M*, posterior papillary muscle; *R V*, right ventricle; *S*, scroll muscle; *T*, tricuspid valve. The electrocardiograms are redrawn to scale; the muscle sketches are diagrammatic.

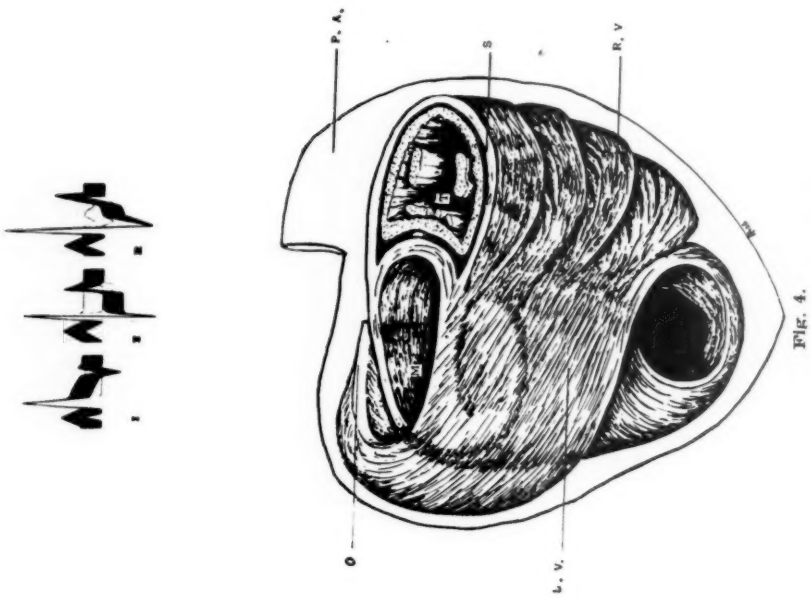

Fig. 4.

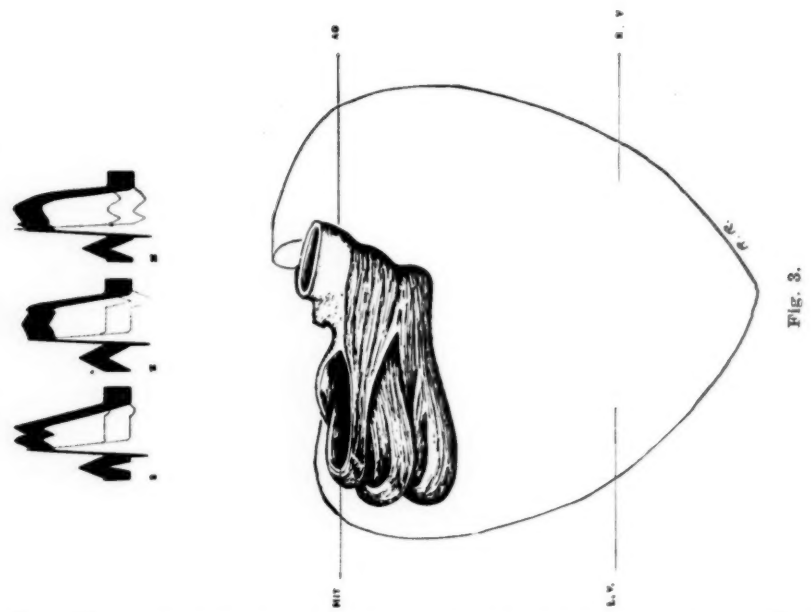

Fig. 3.

Fig. 3.—Deep bulbospiral muscle, posterior view. A constrictor muscle surrounding the base of the left ventricle. Blood supply from branches of the left circumflex. The characteristic electrocardiogram for injury to this muscle shows marked elevation of R-T in all leads.

Fig. 4.—Deep sinospiral muscle, posterior view. Origin, nearly the whole circumference of both A-V rings. Insertion, into all papillary muscles of the right ventricle and to the anterior wall of the left ventricle by fusion with the superficial sinospiral. Blood supply from a branch of the anterior descending coronary and from lateral branches of the right coronary. The characteristic electrocardiogram from injury to either the right or left portion of the muscle shows an elevation of R-T in Lead I and a depression of R-T in Leads II and III.

We have been fortunate in having some human material to study correlating specific muscle lesions with their electrocardiographic manifestations, and at the present time we are of the opinion that the result of experimental work on dogs will eventually be confirmed in man. Because of the fact that the human heart, in order to be of any value to us, must have a lesion in one muscle only, must have an early electrocardiogram, and must then come to autopsy, and at the autopsy the heart must be given to us intact so that we can inject it and study it by very careful dissection, our material is necessarily very limited. An ordinary postmortem heart examination not only is of no value for muscle localization, but very definitely prevents a proper study of the case. A plea is therefore made that wherever material is available it be studied with special reference to lesions in the various muscles, for only in this manner can it be determined whether our experimental findings are applicable to man.

It would appear that lesions of the two superficial muscles demand less protracted treatment and offer a far better prognosis than do those of the deep muscles.

These experiments on dogs indicate that localization of coronary lesions is possible by the electrocardiograph if one localizes according to the muscle bands. The type of muscle injury is unimportant. Data have been presented previously (Robb[7]) to prove that if any lesion involves all the cross-section of the muscle, a further lesion in another area (still having an adequate blood supply) may cause no further change in the electrocardiogram. Mention has already been made of the fact that the electrocardiogram for elimination of the deep sinospiral is constant regardless of whether the left or right portion of the muscle is involved. These results cannot be explained according to the current description of the physiology of conduction in the ventricle.

CONCLUSIONS

1. Certain coronary branches are "end arteries" to the individual ventricular muscle bands.

2. If such end arteries are ligated, the resulting infarcts affect the electrocardiogram consistently.

3. Elimination of either or both of the superficial muscles alters the blood pressure little or not at all.

4. Elimination of either of the deep muscles causes a marked fall in blood pressure, and if the lesion be large, death is immediate.

5. These results cannot be explained according to present-day conceptions of the physiology of conduction.

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NONPENETRATING WOUNDS OF THE HEART

A Clinical and Experimental Study*

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PROBABLY the most common type of trauma to the heart is that produced by stab or bullet wounds. However, there is another type of cardiac trauma produced by contusive or compressive forces, and it is this type of nonpentrating cardiac wound that we shall discuss in this paper.

One is accustomed to look upon the heart as an organ which almost always escapes any of the ordinary injuries to which the rest of the body is subjected. The thoracic cage affords what is usually considered to be practically a perfect protection to the heart. No such immunity to injury from contusive or compressive forces is extended to the liver, spleen, kidneys, brain, and other organs of the body. It is remarkable that this belief has developed, because the heart, lying against the sternum, is vulnerable to any sudden impact over the sternum and, buttressed against the bodies of the thoracic vertebrae posteriorly, is vulnerable to compression forces applied to the chest. There can be little doubt that the heart is the recipient of many injuries. Most of these probably produce no functional disturbances and are not recognized. Some of them do produce functional disturbances, and usually these are not recognized.

We have attempted to review all cases of nonpenetrating cardiac wounds that have been reported.† The entire literature on the subject, however, was not available to us, so that our study, while extensive, is not complete. We have excluded from our analysis those cases in which the injury produced a rupture of a valve without showing other manifestations of cardiac injury. This group was excluded because a rupture of the valve seems to offer no possibility for operative repair.‡ We have excluded also those cases of rupture of the

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†We are indebted to Dr. J. A. Groh for his assistance in the analysis of the German literature.

‡We do not want to imply that the operative repair of a cardiac valve is entirely beyond the realm of possibility. We should remember that operative surgery, as we know it today, is very young. Although surgery has an ancient ancestry, nevertheless our modern methods of operating are not old. We do not want to underestimate the operative methods that were established centuries ago, but is it not true that surgery just learned to stand up and walk, so to speak, in the 80's and 90's of the last century? And is it not true that the development of some of the more difficult technical procedures, such as some of the intracranial and intrathoracic operations, had to wait twenty-five years until Lister's child learned its alphabet? It is not inconceivable that technical methods may develop so that operations can be done, not only on the surface of the heart as they are today, but also in the cavity of the heart.

heart that followed myocardial infarction due to coronary occlusion. This group was omitted because the rupture in cases of myocardial infarction is not traumatic in origin. The group of cases designated as cardiac strain also was excluded. This group may be related to the general one of nonpenetrating trauma so far as the possible rôle of increased intracardiac pressure is concerned. The symptoms may be similar, but evidence of trauma is not demonstrable at autopsy in cases of heart strain.

On the basis of our analysis we can give in outline form the various ways by which nonpenetrating wounds of the heart were produced.

I. A direct blow over the precordium producing fracture of sternum or ribs, the broken ends of which were driven into the heart.
   a. A cavity of the heart may be penetrated (Heger-Houbotte).
   b. The myocardium may be penetrated, rupture taking place days, weeks or months later (Groom), or the wound may heal with recovery or an aneurysm of the heart may develop later (Joachim and Mays).

II. Contusion or compression of the heart between the sternum anteriorly and the vertebrae posteriorly. This space is occupied almost entirely by the heart, and any decrease in it directly affects the heart.
   a. The heart may be ruptured. The ribs and sternum may be fractured (Kennedy, Ferris), or they may not be fractured (McOscar and Voelcker, Hutchinson, Godlee, Bilderbeck).
   b. The heart may be bruised but not ruptured, and it may or may not show functional derangements later.

III. The application of indirect forces, such as by the sudden compression of the legs and abdomen (Kellert, Stephens, Copeland).

IV. Laceration of the thoracic viscera, such as may be sustained in a fall from a high building (Robertson, Heger-Houbotte, Schütt).

V. Concussion of the heart. Although this term has been used by several writers, we are unable to determine from the literature whether the heart can be disturbed by concussive forces. The distinctive feature of a concussive injury is that it is usually produced by a force of rapid motion without bringing about demonstrable pathological changes. One can assume that functional alterations in the conduction mechanism of the heart may take place without showing organic changes. It is possible that stimuli resulting from trauma and transmitted through the vagus nerves can stop the heart. In the case reported by Lee and Downs the heart stopped when traction was exerted upon the stomach. In the case reported by Glover the heart stopped when a gland was dissected from the root of the

mesentery in the duodenojejunal angle. These probably were instances of vagus stimulation.

The cases that we analyzed can be classified into three groups: (1) the group of patients that survived the trauma; (2) the group that died of myocardial failure; (3) the group that died of rupture of the heart.

GROUP I. PATIENTS WHO SURVIVED THE TRAUMA

Inasmuch as the patients in this group survived the trauma, the diagnosis of cardiac involvement was made on clinical manifestations. The group includes twelve cases.

CASE 1.—Hochhaus, quoted by Loison. Case briefly referred to by Loison was a man forty-three years old who was struck by a plank and sustained fractures of several ribs. Circulatory decompensation developed after the accident, but the patient recovered.

CASE 2.—Lückinger, 1893. Patient, a male twenty-five years old, fell from a load of straw and struck the left side of the chest. No evidence of fractured ribs or sternum. Five days after the fall patient developed dyspnea and palpitation of the heart. A pericardial friction rub and a systolic and a diastolic murmur could be heard. On the following day these signs and symptoms disappeared, and the patient recovered.

CASE 3.—Moullin, C. W. Mansell, 1897. Patient, a male twenty-three years old, was injured while playing football. The injury was inflicted by an opponent's elbow striking against the third left intercostal space. He continued with the game for twenty minutes after the accident. Then he collapsed. Twenty-five days after the accident the patient was critically ill. The area of cardiopericardial dullness had increased, the cardiac sounds were distant, cyanosis was marked. An incision was made in the fifth interspace on the left side and the pericardium incised. Six pints of thin, dark fluid were removed from the pericardial cavity. Patient recovered and was in good health.

So far as we have been able to determine, this was the only case of nonpenetrating injury in which the operation of pericardiostomy was carried out. In this respect it is unique. Whether the heart sustained a bruise was not determined by the operation. It would seem that the exposure was too limited to afford adequate examination of the heart to determine whether or not there was a contusion of the myocardium. Experimentally a hemorrhagic effusion not uncommonly develops after the myocardium has been bruised.

CASE 4.—Rosenson, 1924. Patient was a boy ten years old who three years before had received a hard punch over the precordium. Immediately after the trauma the child became weak and experienced a fluttering sensation in the region of the heart. He was unable to walk. Two days later he attempted to walk, fell, and became unconscious. Examination showed pallor of the skin, slight dyspnea, and a heart of normal size. The electrocardiogram showed partial (?) heart-block, a rapid ventricular rate, P-R interval 0.28 second, P- and T-waves fell together. The patient was kept in bed for two weeks, and at that time the heart returned to normal rhythm. During a three-year period of observation the heart remained normal. The author asks the question whether the lesion in this case was a slight hemorrhage in or about the node of Tawara, and he makes the comment that there is no similar case reported in the literature.

CASE 5.—Levison, 1927. Patient was a male twenty years old who received a crushing injury to his chest, having been compressed between two trucks. There were no fractures. The patient immediately had severe pain over the precordium, marked dyspnea but no cyanosis. Auricular fibrillation with a pulse rate of 150 per minute developed. Dyspnea was increased by exertion. The electrocardiogram taken thirty-six hours after the accident showed normal mechanism, and abnormally large T-waves in all leads. The patient made a complete recovery. All signs and symptoms of a cardiac nature disappeared.

CASE 6.—Yates, 1916. Patient was a farmer, forty-six years old, who was thrown out of a wagon by a runaway team. The fourth and fifth ribs on the left were fractured. The chest wall was depressed over the axillary region on the left side. The patient complained of pain in the chest. He had marked dyspnea. A loud splashing sound was heard with each heartbeat, and it was believed that hemopneumopericardium was present probably from a rib penetrating lung and pericardium. This sound persisted for ten days. The patient was critically ill for two weeks. He then recovered and was up and about three weeks after the accident.

CASE 7.—Kahn and Kahn, 1929. A woman thirty-two years old weighing only 82 pounds slipped and fell forward, striking the sternum against the corner of a table. Immediately after this accident she felt severe, sharp pain in the precordium. Tachycardia, dyspnea, and palpitation of the heart also developed. These symptoms were sufficiently severe to make the patient go to bed. Six months after the accident she still had marked precordial and sternal tenderness, dyspnea, palpitation of the heart on exertion, a murmur heard at the apex, and disability due to the sternal pain. The electrocardiogram was normal. The authors did not claim that this case necessarily was an example of a cardiac contusion.

CASE 8.—Kahn and Kahn, 1929. A man, fifty-five years old, was hit over the left lower ribs by a truck. He was unconscious for a short period of time; he had intense pain in the left lower abdomen, and an aching, numb sensation in the left hypochondriac region. That night the sharp, localized pain in the left lower ribs became worse, especially on deep breathing. He was dyspneic and had palpitation. Two days later pleurisy was diagnosed. One month after the accident the patient had a sudden severe localized gripping pain over the left lower ribs. Similar attacks of pain were accompanied by palpitation of the heart and dyspnea. Four months after the accident the patient was well except for tenderness to pressure over the cardiac apex. "Apparently the injury produced no permanent affection of the heart, although the symptoms and the attacks that the patient suffered from may be attributed to some direct trauma to the heart."

CASE 9.—Kahn and Kahn, 1929. This patient was a man forty-nine years old who tripped and fell heavily to the ground. Later in the day he felt some tightening in the chest and had a little difficulty in breathing. That evening he had dyspnea, which was worse the next day. "He remained in bed for a month after the diagnosis of acute pericarditis was made." A month after the accident he had dyspnea and a slow pulse of small volume. The heart sounds were somewhat muffled. The brachial arteries were somewhat tortuous. The electrocardiograms showed normal sinus rhythm, left ventricular preponderance, inversion of the T-wave in Lead I, and the P-wave isoelectric in Lead III. The patient "resumed lighter work for five months or more before he died rather suddenly [i.e., about ten months after the accident]. Whether or not the coexistence of acute coronary closure figured in its production must remain speculative."

CASE 10.—Kahn and Kahn, 1929. A man thirty-three years old was struck over the front of his chest by a plank of lumber which fell from a scaffold 18 feet above the ground as the patient was looking up. The patient fell backward, was momentarily dazed, got up but was so weak that he had to lean against the building. He had dyspnea, and as he walked he was weak and dizzy. He worked half of the following day. He spent the next two weeks in a hospital. Examination three months after the accident showed auricular fibrillation with a rate of 150 per minute. "There was an indication of left ventricular preponderance. Premature beats occurred singly or in groups, arising probably in the auricular wall in the region of the A-V node." The arterial pressure was 104 mm. Hg systolic and 78 mm. diastolic. Normal sinus rhythm was restored after the administration of quinidine sulphate. Six months after the accident recovery was complete. All symptoms had disappeared. The authors stated that "the pathological changes that may have taken place from the injury are necessarily speculative. The possibility of subepicardial ecchymosis in the auricular muscle is to be considered."

CASE 11.—Kahn and Kahn, 1929. A truckman sixty-three years old while lifting a heavy weight fell and struck his chest on the end of a wagon. He was unconscious for a few minutes after the accident and then resumed his work. For the next two days he was in bed; his condition became worse, and four months after the accident he was placed in a hospital. At that time he had auricular fibrillation. Myocardial failure resulted in death five months after the accident. The authors concluded that "the patient showed arteriosclerotic myocardial disease and auricular fibrillation. If the fibrillation had existed prior to the injury, the man would have had some distress or inability to do his work. In the absence of this we are compelled to attribute the onset of fibrillation to the direct trauma to his chest that he suffered in the fall."

CASE 12.—Tuohy and Boman, 1931. A man seventy years old while carrying a weight of 100 pounds on his shoulder tripped and fell down a stairway, striking his thorax a stunning blow. He was not unconscious. He suffered severe precordial pain. There were no fractures. An electrocardiogram taken five weeks after the accident showed complete heart-block. One taken after another interval of five weeks showed normal sinus rhythm but right bundle-branch block. This condition lasted for about ten days, when complete block returned. The authors present this query, "What was the relationship of his injury to this decisive interference in his conducting mechanism? The answer could be more dogmatically given could the interventricular septum be carefully examined. Two general hypotheses present themselves: This seventy-year-old man came by his conduction disturbance through the usual route of myocardial fibrosis with localization in the interventricular septum and affecting the bundle of His independent of his injury; or the injury induced traumatic sequences, the most likely of which is hemorrhage into the same area."

GROUP II. PATIENTS WHO DIED OF MYOCARDIAL FAILURE

This group includes those cases in which death occurred from myocardial failure. The diagnosis was made by necropsy examination. The group consists of 11 cases. The cases reported by Blancard (1688) and Akenside (1764)—both quoted by Fischer—were excluded from this group because it could not be determined whether trauma or infection was responsible for the changes in the heart.

CASE 1.—Watson, quoted from Fischer. We were unable to find this article. The case was referred to briefly as one in which the sternum was fractured, the pericardium torn, and the myocardium bruised.

CASE 2.—Casper, 1857, quoted from Fischer. A male, sixty-six years old, was knocked down by a falling sack of corn. One femur was fractured and the leg was amputated. Death occurred eight days later. The necropsy examination showed fractures of the third thoracic vertebra and several ribs. An extensive hemorrhagic area in the wall of the left ventricle was found, measuring about 2 inches in diameter.

CASE 3.—Markham, 1858. This patient was a man who was injured in a fall from an omnibus. Death resulted from hemorrhage in the brain. A bruise the size of a silver dollar was found in the interventricular septum.

CASE 4.—Werner, 1873. This patient was a child three years old who was ground under foot by a cow and died thirty-one hours after the accident. The pericardium was intact; there was no intrapericardial hemorrhage. Extravasation of blood was found under the epicardium. The myocardium was completely severed on the anterior wall of the left ventricle, leaving only the epicardium intact. Apparently the epicardium alone prevented the escape of blood from the cavity of the heart. The tear of the myocardium measured 14 mm. in length.

CASE 5.—Schuster, 1880. A healthy laborer, forty-three years old, received a blow on the chest by a harness bar and was thrown violently to the ground. He immediately recovered, but for a period of two weeks he had pain in his chest. While doing some heavy lifting he developed severe epigastric pain and a sensation of choking. The skin became pale, cold, and cyanotic. The pulse became weak and the patient died two hours after the exertion. The necropsy examination showed some extravasation of blood in the mediastinum and in the pericardial cavity. The left ventricular wall and the right auricular wall showed extravasation of blood. The right coronary artery and vein were surrounded by hemorrhage. According to the description these vessels were encroached upon by hemorrhage.

CASES 6 and 7.—Rose, 1884, quoted from Loison. One patient was a man forty-six years old who was injured by a carriage wheel passing over the chest. He became unconscious and expectorated blood. Two ribs were fractured. On the fourth day after the accident the patient died, and at autopsy a wound of the left ventricular wall was found. The wound was situated on the anterior surface of the ventricle and did not penetrate the cavity of the heart. There was also a small perforation of the pericardium, and the left lung was lacerated. The other patient was a man thirty-four years old who fell from a height of 14 meters. This patient became unconscious and died several hours after the accident. At autopsy a wound of the left ventricle was found. It did not penetrate into the cavity of the ventricle. The pericardium and the lung were lacerated.

CASE 8.—Potain, 1892. A man, forty years old, was struck over the third rib on the left by the shaft of a wagon. The patient became unconscious for a few minutes after the accident. He complained of pain where he was struck. One month after the accident he had palpitation of the heart, dyspnea on exertion, an irregular pulse, some enlargement of the heart, and a presystolic murmur. The patient died thirteen months after the accident. The examination showed an aneurysm at the apex of the heart, some dilatation of the conus arteriosus, and chronic myocarditis.

CASE 9.—Thiem, quoted from Ercklentz, 1910. This patient was a male who was kicked on the left side of the chest by a horse. For a period of two weeks following the accident the patient suffered with a feeling of substernal oppression and impending death. He also had sharp pain radiating down the left arm. Fifteen months later he died in an anginal seizure. The examination showed evidence of "old hemorrhages" in the interventricular septum.

CASE 10.—Vaquez, 1924. This patient received a violent blow in the region of the base of the heart by a carriage pole. Death occurred several months later, and an aneurysm in the region of the conus arteriosus was found.

CASE 11.—Joachim and Mays, 1927. This patient was a male, twenty-five years old. At the age of twelve years he had been run over by a wagon, and several ribs on his left side were fractured. At the age of twenty-three years he began to have severe attacks of paroxysmal tachycardia with a cardiac rate of 170 to 200 per minute. These attacks lasted for periods varying from ten minutes to one week and were accompanied by cyanosis, pulmonary edema, and congestion of the liver. He died suddenly at the age of twenty-five years. The autopsy showed an aneurysm of the left ventricle on the anterior wall near the apex. The myocardium at the base of the aneurysm was atrophic.

GROUP III. PATIENTS WHO DIED OF RUPTURE OF THE HEART

This group consists of 152 cases of cardiac rupture. The diagnosis was established by necropsy. An analysis of these cases showed that rupture of a cardiac chamber occurred in one of three ways.

I. Bursting of the heart by compressing it between the sternum and vertebrae much as a toy balloon can be compressed in one's hand. It would seem that this compression would be more destructive if it were applied at the moment when the heart is filled with blood and is beginning to contract as at the end of diastole and at the beginning of systole. It would also seem that the compression would be more destructive if it were applied from the base of the heart toward the apex, thus preventing the blood from leaving the heart through the great vessels. Another factor in this type of injury is the marked friability of living cardiac muscle to abnormal forces. It is easily cracked and broken, and it would seem that the myocardium would break open if the heart were flattened out against the vertebrae even though it were empty and relaxed.

II. Contusion of the heart with subsequent softening of the area of contusion (Howat, Kugel, O'Neill). Rupture takes place hours, days, weeks or months later. The intracardiac pressure is increased by physical exertion, and the bruised myocardium blows out when the patient exerts himself.

III. Increased intracardiac pressure. This may be brought about by the application of forces directly to the heart as already referred to (Stephens, Ferris, Peacock), or it may be produced by the application of indirect forces as by sudden compression of the legs and abdomen (Kellert, Saphir).

That the heart and pericardium can be ruptured by the sudden application of a compression force limited to the abdomen and lower extremities seems to be impossible on a priori considerations. Nevertheless, Kellert reported the case of a man who was engaged in digging in a sand bank when suddenly the sand bank caved in and he was engulfed up to his waist. When he was dug out, he was dead. A laceration 5 cm. in length extended through the interventricular septum and opened both ventricular cavities. The endocardium of the right auricle was lacerated. The pericardium was ruptured. Microscopically there was some fatty infiltration of the right ventricular wall, vacuolization of the muscle fibers, and an occasional area of fibrosis. According to Kellert, "There are two possibilities in explanation of the lesion in the present instance. First, that the weight of the falling earth which, being soft and adaptable, caused equal pressure over the chest resulting in great compression and bursting of the heart, very much as though a rubber bag distended with fluid were compressed at its middle. To obtain such an effect without fracture of the sternum or ribs seems very unlikely. [However, Kellert stated that the patient was engulfed up to the waist.] The second and more probable explanation is that of hydraulic pressure. The large quantity of sandy soil exerted such great pressure over the lower half of the body as to drive most of the blood out of the vessels. This produced sudden overdistention of the heart, which was probably dilated as a result of physical exertion, with consequent rupture at several points. That the force was a great one is indicated by the ruptured pericardium and hemorrhages in the lung. The pathologic changes in the heart, though not very marked, undoubtedly contributed to the severity of the injury."

Saphir reported the case of a boy, four years old, who was run over by a motor truck. The thoracic wall showed no evidence of injury. The pericardial cavity contained about 300 c.c. of blood. The left ventricular wall was ruptured for a distance of 6.5 cm. The myocardium showed no evidence of disease. The pelvis was fractured. Saphir stated: "While blows to the chest cannot be excluded, we saw no evidence of injury to the chest wall. Therefore the most probable explanation is that the rupture of the heart is dependent on the trauma of which the greatest force was exerted in the region of the right pelvis."

Stephens briefly recorded an example of rupture of the heart as follows: "A well-built lad, aged sixteen, was standing near a crane from which was suspended a heavy steel tube. As the tube was lowered it pressed against his chest and abdomen; he then stepped back a few paces and fell down, dead. Post-mortem examination showed the intrapericardial pressure was atmospheric, and on opening the sac it was found to be full of blood. In the right auricle was a tear one

inch long. Was this due to the back pressure caused by the tube pressing on his abdomen?"

Whether the heart can be injured by such indirect forces could not be answered by any experimental work that we were able to find. Accordingly, we carried out some experiments in which pressure was suddenly applied to the legs and abdomen and the compression effect upon the heart was studied. In these experiments we found that acute cardiac dilatation and failure could be produced, but in none of the experiments was the heart actually ruptured. Small hemorrhages in the epicardium and myocardium were not uncommon. The right auricular pressure showed a marked rise when the legs and abdomen were compressed, and it is probable that under certain circumstances actual rupture takes place in this way.

In the 152 cases of cardiac rupture that we analyzed, the way in which the trauma occurred was mentioned in 105 instances. In 38 instances the patient was run over by a wagon, automobile, or train; in 22 the patient was crushed between two objects, such as a wagon and a wall or two railroad cars; in 17 the patient was injured by a direct blow over the chest as by a club or a fist; in 12 the patient was struck by a falling object; in 8 the patient was kicked on the chest by a horse; in 3 the patient was injured in an explosion; in 2 the injury was sustained from a bullet striking against the sternum; in 1 the injury was sustained in a fall; in 1 the injury was sustained by the patient having been jumped upon by playmates, and in 1 the heart was ruptured when the patient was engulfed in a sand bank.

The largest group of cases (29) consisted of young men between the second and third decades of life. The second largest group of cases (22) consisted of boys between the first and second decades. In the entire group there were 113 males, 12 females, and 21 cases in which the sex was not mentioned.

It is interesting that the four cardiac chambers seem to be equally vulnerable to rupture. The right auricle was ruptured in 36, the left auricle in 30, the right ventricle in 31, the left ventricle in 37, and more than one chamber was ruptured in 13 cases. The interventricular septum was opened in 11 cases, and the interauricular septum was perforated in 1 instance.

It is also interesting to note that in 58 of the 152 cases it was specifically stated that the ribs or sternum, or both, were fractured; and in 88 cases either no mention of associated fractures was made or it was stated that there were no fractures of the thoracic cage. It should be emphasized that the heart can be ruptured by compressive or contusive forces without producing any fractures of the thoracic wall. One would expect this statement to apply especially to those cases in which the chest wall was pliable as in children and women

and men of frail build, but the heart can be ruptured in well-developed men without accompanying fracture of the chest wall.

The most frequent cause of death in this group of cardiac ruptures was neither the injury to the heart per se nor exsanguination. In 76 of the 152 cases of cardiac rupture the pericardium was distended with blood and the cause of death was hemocardiac tamponade. In 23 cases an extensive hemothorax was found. In 15 cases the injuries were extensive and involved other vital parts, and death was instantaneous. In 7 cases death was due to cardiac insufficiency. Two patients died with purulent pericarditis, one had pneumonia and one had pulmonary edema. In 21 cases the report was incomplete and the cause of death could not be determined.

These cases of cardiac rupture resulting from nonpenetrating trauma were analyzed in reference to their clinical manifestations and treatment. Obviously those cases in which death occurred immediately can be excluded from this analysis. They showed the signs of increased intrapericardial pressure or exsanguination into the thoracic cavity or injury to other vital organs. In 47 cases death occurred immediately after the accident, and in 42 cases the interval was not mentioned, but undoubtedly in most instances it was of brief duration. Thus any form of operative treatment was precluded by the time factor alone in 89 of the 152 cases. Out of the remainder of the group we selected those cases in which death did not occur within forty-five minutes or an hour after the accident. The second requirement for a case to be placed in this group was that the injury to the heart was not so extensive but that it might have been possible to repair it at operation. This special group consisted of 30 cases. It is an interesting group to analyze because it presents opportunities for treatment that were not utilized. Inasmuch as operation was not attempted in any of these cases, the group assumes sufficient importance to present it in tabular form, Table I.

If surgery has something to offer in this group of cases, the questions arise as to how the diagnosis can be made, which cases should be selected for operation, and what should be done at operation.

It is apparent from Table I that most patients had a short clinical course. Eighteen died within nine hours after the accident. If the patient survived the first nine hours, his chances of living through the first week were somewhat better than his chances of going through the second week. A possible explanation for this is that the area of contusion is weaker or softer during the second week than it is during the first week and that rupture is more prone to take place at that time. After the second week it would seem that the area of contusion becomes stronger because of the development of scar tissue. In the patients who survived the two-week period we find the duration of life being 30, 39, 49, and 60 days after the accident. Table I also

TABLE I

CASES OF CARDIAC RUPTURE POSSESSING SURGICAL POSSIBILITIES

NAME OF AUTHOR	SEX AND AGE OF PATIENT	TYPE OF INJURY	PATHOLOGY	MECHANISM OF RUPTURE	SYMPTOMATOLOGY	RESULTS
Bérard 1826	Male, young	Fell from a window.	Tear in left auricle. Much blood in pericardial cavity.	Not given.	Not given.	Death 2½ hr. later.
Lees 1837	Male, a brewer	Fell under a dray which passed over his chest.	Rupture of right auricle. Fracture of fifth rib. Blood in pericardial cavity.	Compression of chest.	Pain in chest, weakness. Drove horse for 1 hr., then walked into hospital.	Death 1 hr. later.
South 1839	Male	Run over.	Tear in heart at apex. Fracture of sternum and 2 ribs. Blood in pericardial cavity.	Fifth rib pierced the heart.	Not given. Walked 100 paces.	Death 9 hr. later.
Fenner 1846	Male, 30 yr.	Fell from a window on fourth story to pavement.	Rupture into left auricle, between mouths of pulmonary veins. Fracture right thigh.	Not given.	Prostrate, pulseless, cold. Pain in right shoulder, vomited.	Death 28½ hr. later.
Hewett 1847	Male, 29 yr.	Fell from a ladder.	Rupture of anterior wall of left auricle 0.5 in. long. Pericardium distended with blood.	Not given.	Cyanotic, cold, pulseless, pain in chest.	Death 2 hr. later.
Hewett 1847	Male, middle age	Thrown from a cart, probably run over by it.	Rupture of left auricle and tear in pulmonary artery. Pericardium filled with blood.	Not given.	Collapse.	Death 4 hr. later.
Stanley 1850	Male, 38 yr.	Large iron plate fell on left leg.	Tear in endocardium of right auricle. Small tear into cavity of left auricle.	Not given.	Pulse feeble. Sepsis of leg.	Death 12 days later.

TABLE I—CONT'D

NAME OF AUTHOR	SEX AND AGE OF PATIENT	TYPE OF INJURY	PATHOLOGY	MECHANISM OF RUPTURE	SYMPTOMATOLOGY	RESULTS
Macleod 1858	Male, soldier	Hit by round shot on breast plate.	Small rupture of left ventricle. Pericardium contained 2 oz. of blood.	Not given.	Walked to rear. Acute pain in region of heart.	Death 72 hr. later.
Cregeen 1859	Male, 38 yr.	Piece of iron fell on head.	Rent in anterior aspect of right auricle. Pericardium filled with blood.	Not given.	Headache.	Death 2 months later.
Sprakeling 1873	Male, 45 yr.	Knocked down by butcher's cart.	Laceration of left auricle. Pericardium filled with blood.	Not given.	Shock, soreness over injury. Heaving chest.	Death 8 hr. later.
Cleghorn 1873	Male, 28 yr.	Struck by lathe on left breast.	Rupture of apex entering left ventricle. Pericardium filled with blood.	Heart supposedly contracted and in contact with chest wall when blow was struck.	No external signs of violence.	Death 2 hr. later.
Heydenreich 1880	Male, 47 yr.	Chest caught between locomotive and stationary object.	Tear 3 cm. long into right auricle. 300 c.c. of blood in pericardial cavity. Fracture of sternum.	Severe compression of chest.	Loss of consciousness.	Death in 2½ hr.
Christiani 1889	Male	Not known.	Nonpenetrating wound of heart.	Wound which perforated after 39 days during violent exercise.	Not given.	Death in 39 days.
Hutchinson 1894	Male, 59 yr.	Kicked by a horse.	Tear into right ventricle, ¾ in. Rent in pericardium and blood in pleural cavity.	Direct violence.	Collapse, pain in cardiac region, pulse slow, regular, low blood pressure.	Death in 3¾ hr.

TABLE I—CONT'D

NAME OF AUTHOR	SEX AND AGE OF PATIENT	TYPE OF INJURY	PATHOLOGY	MECHANISM OF RUPTURE	SYMPTOMATOLOGY	RESULTS
Webersberger 1894	Male	Kicked by a horse.	Rupture 1 cm. long in wall of right atrium. 750 c.c. of blood in pericardial cavity.	Direct violence.	Vomiting, collapse, shock, pain in precordium. Not able to hear heart sounds.	Death in 1½ hr.
Bennett 1895	Male, young	Explosion of bomb.	Rupture left ventricle. Pericardium distended with blood. Wound in branch of left coronary artery. Fractured ribs.	Direct violence.	Collapse, masked heart sounds.	Death in 2½ hr.
Robertson 1897	Male, 49 yr.	Fell from open door of a railroad carriage.	Laceration of left auricle. Pericardium distended with blood clot. Normal heart muscle.	Violent impact of left shoulder. Direct violence.	Walked to work 200-300 yd. Sudden collapse.	Death in ¾ hr.
Groom 1897	Male, 16 yr.	Accident with runaway pony. Struck chest against a fish-trap.	Hole the size of a little finger in left ventricle. Pericardium filled with blood.	Incomplete tear of myocardium. Aneurysm which broke suddenly.	In bed 5 days, weak, sudden collapse.	Death in 1 month.
Gibbons 1897	Male, 30 yr.	Struck across chest with bamboo stick.	Small rupture in right ventricle. Pericardium distended with blood.	Direct violence.	Pain in left side. In hospital.	Death in 3 hr.
Newton 1898	Male, 28 yr.	Fell on handlebar of bicycle.	Tear in apex of right ventricle. Pericardium contained 10 oz. blood. Fracture of left 6th costal cartilage.	Direct violence.	Pain in left side. Collapse, failing pulse.	Death in 1½ hr.

TABLE I—CONT'D

NAME OF AUTHOR	SEX AND AGE OF PATIENT	TYPE OF INJURY	PATHOLOGY	MECHANISM OF RUPTURE	SYMPTOMATOLOGY	RESULTS
Ebbinghaus 1902	Male, 12 yr.	Fell from window six floors to the ground.	Rupture into the left ventricle. Pericardium distended with blood. Myocardium softened about rupture.	Contusion of myocardium with subsequent softening.	Unconscious. Cardiac dullness normal. No symptoms after 3 days until sudden collapse 9 days later.	Death 9 days later.
Kugel 1909	Male, 14 yr.	Struck by a heavy bale of goods.	Rupture of right atrium. 500 c.c. of blood in the pericardial cavity.	Forceful rupture of heart. Question of strain from heavy lifting.	Coma, immediate collapse, pulseless, cold and clammy.	Death 42 hr. later.
Corin 1911	Male, 63 yr.	Crushed by a wagon loaded with coal.	Transverse tear into left ventricle. Pericardium distended with blood.	Vertebral column acted as a wedge. Left heart distended at time of compression of thorax.	Examination negative, told to return to work. Sudden collapse.	Death 5-6 hr. later.
O'Neill 1914	Male, 9 yr.	Knocked down and jumped on by boys while playing.	Perforation 3 mm. long in right auricle. 700 c.c. of blood in pericardial cavity.	Rupture first, then sealed off and then broke loose again.	Pain in left side. In bed for 2 days. Sudden collapse 5 days later. Death 1 hr. after collapse.	Death 7 days later.
Kennedy 1914	Female, 60 yr.	Knocked down by a cart shaft which struck right mammary region.	Two small ruptures into left ventricle. 10 oz. of fluid in pericardial cavity. Fracture of sternum and ribs.	Rupture by bursting.	Not given.	Death 1 hr. later.

TABLE I—CONT'D

NAME OF AUTHOR	SEX AND AGE OF PATIENT	TYPE OF INJURY	PATHOLOGY	MECHANISM OF RUPTURE	SYMPTOMATOLOGY	RESULTS
Turner & Gould 1917	Male, 47 yr.	Fell 20 ft. from ship against a buoy.	Small tear in anterior wall of right ventricle. Fracture of sternum. 15 oz. of blood in pericardial cavity.	Rupture at time of accident, clot which later gave way. Direct violence.	Unconscious, shock. Heart sounds distant. Conscious at 5 hours. Sudden collapse.	Death 7 hr. later.
Howatt 1920	Male, 68 yr.	Chest squeezed by truck against an iron pipe.	Left ventricle bruised in 5 places, apex ruptured. Pericardial cavity full of blood.	Bruise of cardiac muscle which ruptured later.	In bed 2 weeks. Resumed work for 3 weeks. Pain in chest on exertion. Sudden collapse.	Death 7 weeks later.
Reid 1922	Female, 5 yr.	Fell from porch two feet, striking corner of cement step	Rupture of left auricle. Pericardium filled with blood. Blood in pleural cavity and in left lung.	Question of bruise of cardiac muscle and later rupture.	Examination negative at time of injury. Sudden collapse seven days later.	Death 7 days later.
Tuohy & Berdez 1926	Male, 11 yr.	Struck by an automobile.	Small perforation at the apex of left ventricle. Pericardium distended with blood.	Compression of thorax.	Shock, pulse rapid, heart sounds scarcely audible. 2 hours later heart sounds more distant. Pulse slow.	Death 3 hr. later.
Tuohy & Berdez 1926	Male, 63 yr.	Automobile accident, thrown against steering wheel.	Rupture, one inch long, in wall of left ventricle. Pericardial cavity full of blood.	Bruise of myocardium. Increased blood pressure while laughing caused rupture.	Distress in chest, frequent vomiting, sudden collapse.	Death 2 weeks later.

shows that the cause of death in the entire group of cases with one exception (exsanguination) was increased intrapericardial pressure. Several cases showed some contusion of the myocardium in addition to the hemopericardium. In this entire group of cases the opening into the cardiac chamber was not extensive, and the bruising of the myocardium was slight or absent.

The most prominent group of clinical manifestations in these cases was the sudden collapse. The patient may complain of precordial pain, or the pain may be referred to the heart to the left side or to the shoulder. The pulse may be slow or rapid, but as the pressure in the pericardial cavity increases, the pulse becomes feeble. Vomiting and headache may be present. The patient may be restless, he may show great anxiety and may develop air hunger. The vasomotor center makes a heroic effort to maintain an adequate arterial pressure. It is able to do this even when the output of the heart is reduced 50 per cent of the normal (Beck and Isaac). A point is finally reached when the blood in the venous reservoirs can no longer break through the intrapericardial barrier. The skin becomes cold and blanched, some cyanosis may be present, but pallor is more conspicuous than cyanosis, the blood pressure falls, and unconsciousness supervenes. The cardiac sounds become distant and may not be audible. There may or may not be any demonstrable increase in the extent of the cardiopericardial dullness. To take an x-ray picture of the heart may be a waste of valuable time if it should delay an urgent operation. The venous pressure is a good index of the intrapericardial pressure. The height to which the venous pressure rises in cases of cardiac rupture or in stab wounds of the heart cannot be given because such determinations have not been made. Such data would be valuable because the venous pressure might be a guide as to when operation is indicated. Experimentally when the intrapericardial pressure is acutely elevated, the heart is brought to a standstill when the venous pressure is elevated 13 to 15 cm. of physiological solution of sodium chloride. However, if there is active and continuous bleeding in the pericardial cavity, the condition is one of great urgency, and time does not permit the determination of the venous pressure. A definite diagnosis of bleeding into the pericardial cavity can be made by tapping the pericardial cavity with a needle. Indeed, it might be possible by removing some of the blood in this way to keep the patient alive until the operation can be done.

EXPERIMENTS

In order to study the effect of contusions of the heart, we carried out a series of twenty-five experiments the results of which we herewith report. Male dogs were selected weighing from 17 to 25 kilograms. These were trained to lie quietly so that electrocardiograms

could be taken. The size of the heart was determined by x-ray examination. Ether anesthesia was used. The heart was exposed under aseptic precautions from either the left or the right side. The pericardium was incised. The cardiac rate was determined. In five experiments the left femoral artery and the left jugular vein were cannulated and connected to a mercury manometer and a water manometer respectively. The myocardium was then bruised. Usually this was done by striking the myocardium with a metal dilator weighing 40 grams. Repeated strokes with the dilator were applied to a localized area over either the right or the left ventricle. In a few of the experiments hard blows were given to the myocardium with a considerably heavier instrument. Three deaths occurred while the heart was being traumatized, one from rupture and two from ventricular fibrillation. In one experiment 10 c.c. of blood and in another experiment 20 c.c. of blood were injected into the interventricular septum. After these various forms of trauma were applied to the heart, the pericardium was sutured and the wound in the thoracic wall was closed.

Observations: The immediate response of the heart to this trauma was an increase in the pulse rate. The tachycardia frequently became so rapid that the rate could scarcely be counted. A rate of 160 to 180 per minute was not unusual. Occasionally the pulse rate became somewhat slower, and in a few instances the rate decreased and then became rapid. The arterial pressure showed wide fluctuations at the time the myocardium was being traumatized. The pressure momentarily dipped down from about 100 or 120 mm. Hg to 40 or 50 mm. Hg, and then after the application of trauma was discontinued, the arterial pressure usually ran along 20 to 50 mm. Hg below the normal level. Sometimes the arterial pressure made a complete recovery to the normal level. The venous pressure rose 10 to 15 cm. of water while the myocardium was being traumatized, but after the application of trauma was discontinued, the venous pressure returned to normal. The myocardium became swollen and discolored after it was bruised. This was due to extravasation of blood into the myocardium. It was surprising to us to see the amount of trauma that the myocardium could tolerate. Not infrequently the myocardium was bruised to such a degree that one would expect softening and rupture to take place. Rupture of the heart did not occur in any of the survival experiments. In two experiments the heart went into ventricular fibrillation at the time the trauma was applied. In these experiments the heart did not recover its normal rhythm after it began to fibrillate, and death occurred. In each of these experiments an extensive extravasation of blood was found in the interventricular septum. In one experiment death occurred from cardiac failure a few hours after the operation was completed. In the survival experiments, after the

effects of the anesthetic wore off, the pulse rate remained rapid, and the cardiac sounds were faint and distant. In several of the experiments the cardiac sounds could not be heard for several days after the operation; in others the cardiac sounds had a rapid "tick-tick" quality. This was quite characteristic and helped us later to recognize clinically a cardiac contusion in a human patient before death. Even though the cardiac sounds were scarcely audible and the pulse rate was rapid, the dog appeared like any other dog when one approached his cage. He stood up and showed the usual activity, but he was not allowed to exercise, and we cannot make a statement as to how the dog could tolerate activity after a contusion of the heart was produced. Undoubtedly the circulatory reserve was decreased. One dog died of cardiac failure forty-eight hours after the experiment. At necropsy

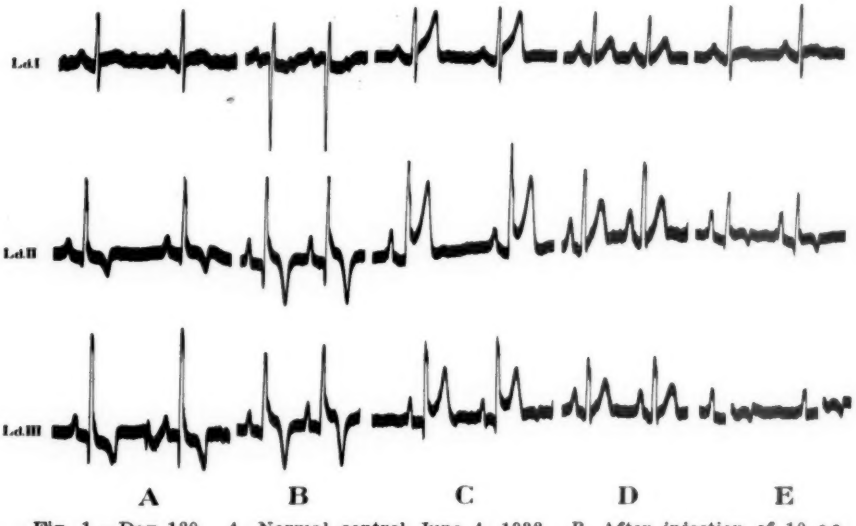

Fig. 1.—Dog 120. *A*, Normal control June 4, 1932. *B*, After injection of 10 c.c. of blood into interventricular septum June 11. Deep Q in Lead I; S-T in Leads II and III slightly everted. T in Lead I diphasic; sharply inverted T in Leads II and III. *C*, June 18, S-T in Leads I, II and III elevated with sharply everted T-waves of increased amplitude. *D*, June 24, T large in amplitude in all leads. *E*, July 13, T in Leads II and III diphasic.

50 c.c. of blood-stained fluid were found in the pericardial cavity, and the heart and the parietal pericardium were adherent at the site of the contusion.

The size and contour of the heart were determined by x-ray pictures standardized as to distances of plate and target from the heart so that comparisons of the shadows could be made. In three-fourths of the experiments cardiac dilatation was demonstrated and the cardiopericardial shadow had an indistinct boundary. This enlargement usually persisted for two or three weeks, when it returned to the normal size, and the outline of the shadow again became distinct. In about one-half of the experiments a blood-stained pericardial ef-

fusion was demonstrable either by tapping the pericardial cavity or by x-ray examination. Occasionally the cardiopericardial shadow remained somewhat enlarged for a month after the trauma. In about

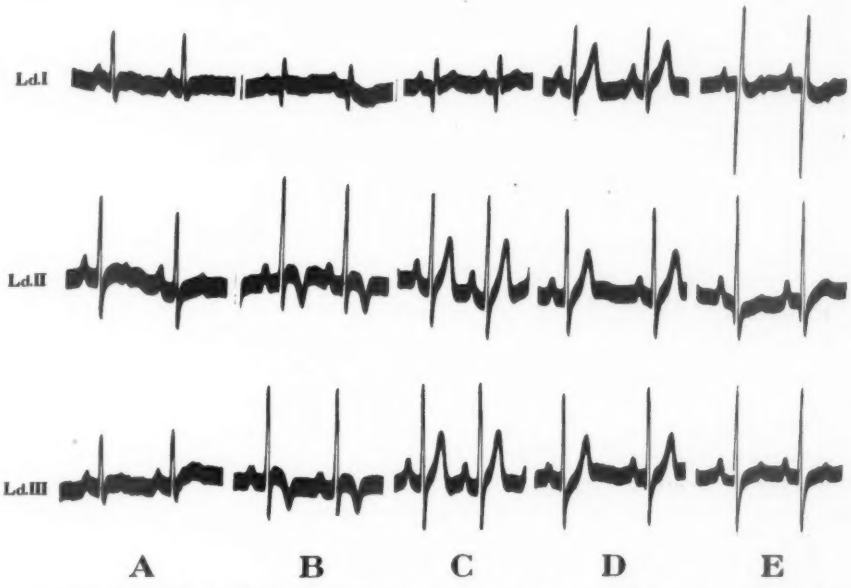

Fig. 2.—Dog 73. *A*, Normal control April 24, 1932. *B*, After 14 blows to left ventricle May 14. S-T in Leads I and II slightly everted, T in Leads I, II and III inverted with sharp angulation, Q in Lead III appeared. *C*, May 21, Q in Lead I; T upright in all leads (large amplitude in Leads II and III). *D*, May 28, T upright in all leads with large amplitude. *E*, June 16, Q in Lead I deep; diphasic T in Lead I; T in Leads II and III upright but of low amplitude.

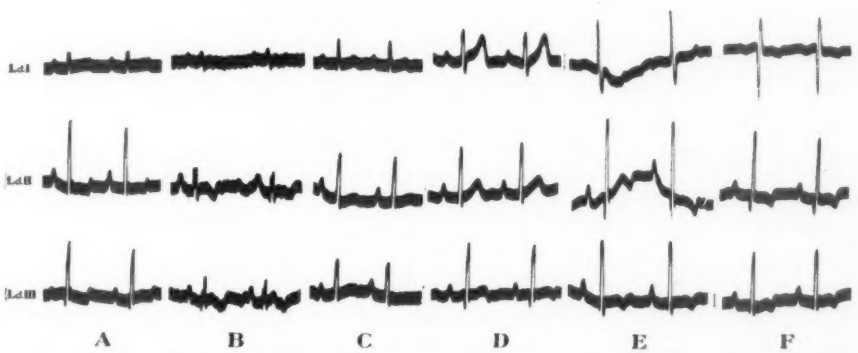

Fig. 3.—Dog 76. *A*, Normal control April 22, 1932. *B*, After 50 blows to left ventricle near apex May 10. QRS of low amplitude; S-T in Leads II and III slightly everted; T in Leads II and III inverted. *C*, May 14, QRS of greater amplitude; T upright in all leads. *D*, May 21, T in Leads I and II increased in amplitude. T in Leads II and III diphasic. *E*, June 4, QRS complex shows increase in amplitude in all leads. T in Lead I upright, T in Leads II and III diphasic. *F*, June 16, deep Q in Lead I, T inverted in Leads I and II, diphasic in Lead III.

one-fourth of the experiments the size and contour of the cardiopericardial shadow did not change from the normal. In clinical cases we believe that if a blood-stained effusion can be demonstrated by aspira-

tion of the pericardial cavity after an injury, one can consider this as evidence in favor of a cardiac contusion.

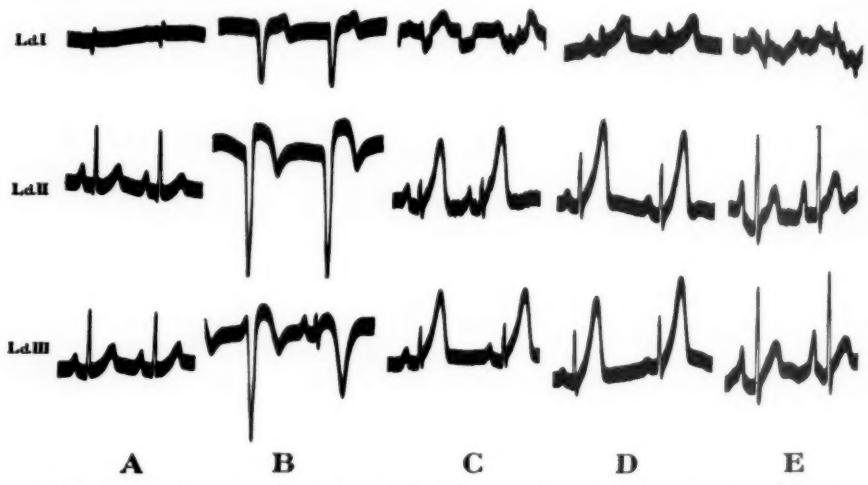

Fig. 4.—Dog 110. *A*, Normal control May 10, 1932. *B*, After 24 blows to wide area of left ventricle May 14. Ventricular tachycardia. In Lead III one normal beat is seen. S-T in Lead III is slightly everted, and T in Lead III is sharply inverted. *C*, May 21, deep S in Lead I; QRS low amplitude in all leads; T increased in amplitude in all leads. *D*, May 28, QRS back to normal amplitude; T-waves large amplitude in all leads. *E*, June 16, Q-wave appears in Lead I; T inverted in Lead I; T lower in amplitude in Leads II and III.

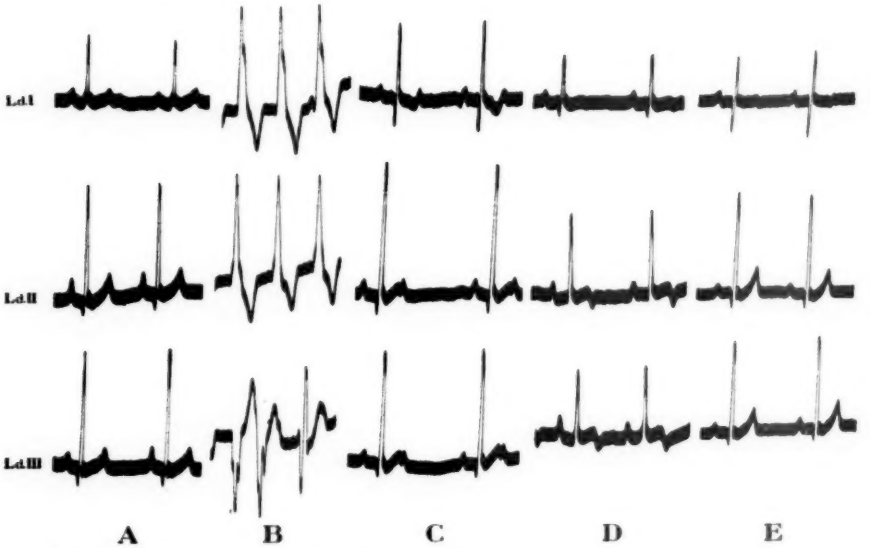

Fig. 5.—Dog 124. *A*, Normal control June 4, 1932. *B*, After 25 blows to right ventricle June 11. Ventricular tachycarda. *C*, June 18, Q in Lead I appears; T in Lead I diphasic; T notched in Leads II and III. *D*, June 24, T in Leads II and III inverted; slight eversion of S-T in Leads II and III. *E*, July 13, deep Q in Lead I.

The cardiac sounds usually remained faint and distant for a period of a week or ten days after the operation. The pulse rate also remained elevated for about the same period of time. Frequently the

normal sinus arrhythmia was lost for two to three weeks, but when the rate became slower it again appeared.

The electrocardiograms in these experiments showed a variety of alterations from the normal. These were analyzed by Dr. Harold Feil and are illustrated in Figs. 1, 2, 3, 4, and 5, and in Table II. The most frequent variation from the normal was the production of large T-waves and alterations in the Q-wave. Frequently there was a high take-off of the T-wave; sometimes the T was inverted. Slurring and

TABLE II

DOG	INJURY	EARLY EFFECTS	LATER EFFECTS
32-120	10 c.c. blood injected into interventricular septum. Post mortem: heart negative.	Deep Q. High take-off of S-$T_{2,3}$, deeply inverted $T_{1,2,3}$ (48 hr.). High take-off Leads I, II, III. Very high $T_{1,2,3}$.	15 days: $T_{2,3}$ very tall. 32 days: Back to normal.
32- 73	14 hard blows to left ventricle near apex. Post mortem: Scar over injury.	48 hr.: Deep Q. $T_{1,2,3}$ inverted. 9 days: Tall $T_{2,3}$.	16 days: Tall $T_{1,2,3}$. 35 days: Deep Q. T back to normal.
32- 76	50 severe blows to apex left ventricle. Post mortem: adhesions between pericardial layers over injury.	Low voltage, slurring QRS in Leads I, II, III.	11 days: Large $T_{1,2}$. 24 days: T_2 sharply negative. 36 days: Deep Q.
32-110	24 blows over left ventricle. Post mortem: numerous adhesions over epicardium.	2 days: Nodal rhythm and intraventricular block (2-1). High take-off S-T in Leads I, II, III. 9 days: High take-off S-T in Leads I, II, III. Very large $T_{2,3}$, QRS low amplitude.	16 days: Large $T_{1,2,3}$. 34 days: Deep Q_1, $T_{2,3}$ high.
32-124	25 blows to right ventricle. Post mortem: Heart negative.	24 hr. Ventricular tachycardia. 8 days: T_1 inverted.	14 days: $T_{1,2}$ inverted. 33 days: Deep Q_1.

notching of the QRS complex occurred frequently. These deviations from the normal electrocardiogram in great part had disappeared after about one month, but some of these alterations persisted for a longer period of time. It is interesting to note that the electrocardiogram obtained in the experiments in which blood was injected into the interventricular septum was somewhat similar to the electrocardiogram obtained in the experiments in which the myocardium was bruised. This, together with the fact that most of the electrocardiographic changes disappeared after a few weeks, would indicate that these alterations were largely due to hemorrhage. The changes in the

electrocardiogram are somewhat similar to the electrocardiographic changes accompanying tamponade, or arterial occlusion with myocardial degeneration due either to arterial or to arteriolar sclerosis.

The animals were killed with chloroform narcosis two or three months after operation. All of them appeared to be in good health before they were sacrificed. It was amazing to us to see how well the myocardial damage was repaired. In three of the specimens there was no trace of the injury to the myocardium, no adhesions and no

Fig. 6.—The heart was exposed at operation, and the myocardium was injured by applying a contusive type of trauma. The damage was repaired by the development of scar tissue at the site of the contusion. The myocardial scar can be seen near the apex of the heart. The entire epicardial surface in this specimen was adherent to the parietal pericardium. In some cases the parietal pericardium seals over the contusion and protects it from rupture.

demonstrable scar tissue formation in the myocardium. In the remainder of the group, consisting of 14 specimens, adhesions between parietal pericardium and epicardium were found. In nine of these the adhesions were limited to the area of myocardium that was bruised; while in the remainder adhesions were generalized but more marked at the site of the injury (Fig. 6). In some of the specimens the adhesions were easily torn apart, but in others the scar penetrated the myocardium. In none of the experiments was the entire thickness

of myocardium penetrated by scar tissue. The scarred area appeared firm and strong, and in no experiment was there any tendency to the formation of an aneurysm of the myocardium. Microscopically the scar could be traced into the myocardium, but nowhere did it replace the entire thickness of the ventricular wall. It was generally confined to the epicardial region. Lymphocytes were found infiltrating the newly formed fibrous tissue and extending also into the subjacent myocardium. Also some small blood vessels were seen in the fibrous tissue.

DISCUSSION

When we began to study this subject of nonpenetrating cardiac trauma, we shared the opinion which we believe is general, namely, that such wounds are exceedingly rare and that so far as clinical manifestations and treatment are concerned the subject is of comparatively little importance. This opinion was changed as the data were assembled. The entire literature was not available, but the number of cases that we were able to analyze was large enough to give an accurate idea of the relative incidence of the various types of such traumas. The important fact brought out by this analysis was that the number of cases that terminated fatally was relatively very high, while the number of cases that recovered was relatively very low. In our analysis of 168 cases death occurred in 157. Of these 157 fatal cases rupture of the heart occurred in 152, or 96.8 per cent, and myocardial failure in 11, or 6.5 per cent. The diagnosis in the entire group of fatal cases was made by necropsy examination. Of the entire group of 168 cases only 12 survival cases were found. This was only 7.1 per cent of the total number. The diagnosis in this group was made on clinical grounds. If these figures can be considered as representative of the true ratio of incidence in cases of rupture, cardiac failure, and recovery, then it can be stated that when the heart receives a nonpenetrating wound, death almost always follows and recovery seldom occurs. Obviously this conclusion is wrong. In the experiments we found that the heart could tolerate a great amount of trauma and that rupture was a rare complication. Experimentally, recovery was the rule rather than the exception. We believe we can conclude from this data that the vast majority of nonpenetrating wounds of the heart are not recognized clinically. These patients recover and only the exceptional one dies of the trauma, showing at necropsy a rupture or a contusion of the myocardium. These exceptional cases find their way into the literature. The other cases in which death does not occur apparently do not receive the correct diagnosis and are not placed in the literature.

We hesitate to try to discuss the subject of diagnosis in this group of cases because the clinical criteria upon which the diagnosis might be based are not infallible. Each of two patients may have been

subjected to similar forms of trauma; both may develop similar clinical manifestations, and these in one may be due to a myocardial contusion and in the other to coronary disease. An accurate differentiation may be impossible. Mistakes can be made in either direction, but the point that we should like to make is that the rôle of trauma is too frequently overlooked. A patient who has been in good health, who receives either direct or indirect trauma to the chest, who then develops symptoms of circulatory embarrassment should, in our opinion, be considered as having sustained a cardiac injury unless other evidence points to a different diagnosis. The heart is not immune to trauma whether the trauma appear to be slight or serious, whether the symptoms be mild and transient or severe and permanent. Naturally an irregularity of the pulse, dyspnea, and anginal pain coming on immediately after an accident in a patient who had no cardiac symptoms previously causes the patient considerable concern and worry. In such cases a diagnosis of cardiac neurosis may be incorrect. Likewise anginal pain and electrocardiographic evidence of a myocardial infarct precipitated by an accident, such as a golf ball striking against the precordium,* are scarcely coincidences.

Although the literature on cardiac contusions consists largely of case reports, a general discussion of the subject is presented by Kahn and Kahn. For purposes of industrial compensation they presented what they considered compensation criteria. These are as follows:

"1. From a labor standpoint, the heart is healthy if a man is able for a long period of time to pursue his occupation without distress and without long periods of absence from work.

"2. If, following direct or indirect violence to the chest, signs of an intrathoracic cardiovascular lesion develop, which are incapacitating, they must be considered the result of an aggravation of a previously existing asymptomatic lesion, or the result of damage to a previously normal heart.

"3. As in heart strain, the time that elapses between the accident and the development of disabling symptoms is very short. There must be immediate pain with its concomitants—dyspnea, rapid irregular pulse, faintness, and cold sweat, and immediate partial or total disability, in order that causal or aggravating relationship be clearly established. Temporary improvement with return to usual or lighter work, followed by a recurrence of the condition, may occur. But in these cases the reappearance of the symptoms and signs should be attributed to the original injury."

We believe that we should make some comment upon the important medicolegal question concerning the interval of time between trauma and onset of symptoms. Kahn and Kahn are definite in their statement that pain, dyspnea, rapid irregular pulse, etc., should develop

*J. A. M. A. 101: 1503, 1933 (Queries and Minor Notes).

immediately after the accident in order to establish causal relationship between cardiac trauma and cardiac symptoms. As already pointed out, almost all cases of cardiac contusion in the literature are cases that terminated fatally. These patients sustained a serious degree of cardiac contusion, and in the cases of this group that were fully reported the symptoms did come on immediately after trauma. In some of the fatal cases the pulse was slow and not rapid. This is a point of difference with the statement by Kahn and Kahn. It is also supported by our experiments. In some of the fatal cases, even though symptoms appeared early, these symptoms gradually became worse over a period of hours, days, or weeks after the accident. In considering cases in which the trauma is less serious, cases in which recovery takes place, the material for analysis is so meager that we hesitate to make a definite statement concerning the possibility of an asymptomatic period after the accident. To support the possibility of a symptom-free period after trauma are the cases of Moullin and of Joachim and Mays. These cases are suggestive of a free period in that the one patient played football after the accident and the other developed paroxysmal tachycardia and an aneurysm of the myocardium years after the trauma. We also know that after a contusion has been inflicted upon the myocardium a process of change takes place in the myocardium. This consists of capillary hemorrhage, infiltration with leucocytes, edema, resolution, and finally scar tissue formation. These changes in the myocardium are progressive, and while their ultimate result is the formation of a scar, nevertheless rupture or an aneurysm may develop subsequently. These complications can produce latent symptoms. On the basis of such data we believe that the onset of symptoms may be somewhat delayed in certain cases of cardiac contusions. Further data are necessary to establish this point.

TREATMENT

The diagnosis of a cardiac contusion having been made, what course will the patient follow? There are several possibilities: (1) the symptoms may disappear hours or days after the accident, and the patient may remain well; (2) the symptoms may persist for years, and they may be accentuated by exercise; (3) the heart may fail hours or days after the accident; (4) the contusion may soften, and rupture may take place. Therapeutic measures can be taken to guard against myocardial failure and cardiac rupture. Obviously these measures consist of absolute rest and the use of morphine or other sedatives as necessary. The heart should be saved as much as possible. Any exertion should be avoided. Mild laxatives should be given, if necessary, to avoid straining at stool. Digitalis may be indicated for the tachycardia or auricular fibrillation. The contusion may rupture any

time during the first month, but most commonly the rupture, if it occurs, takes place during the second week.

According to our analysis of the cases in which rupture occurred, surgical intervention should be considered. When rupture occurs, the need for immediate operation is urgent. For that reason a surgeon should remain in constant attendance; the operating room should be in constant readiness so that the fleeting opportunity to suture the wound can be utilized. Up to the present time operation has not been attempted in any case of cardiac rupture. To Mansell Moullin belongs the credit of having evacuated bloody fluid from the pericardial cavity in a boy who had sustained a nonpenetrating form of trauma. Recovery took place, but the heart was not explored, and it was not determined whether a rupture was present. The hemorrhage in this case might have come from the myocardium or it might have been a hemorrhagic effusion, such as we observed in our experiments.

If there is any evidence of a pericardial effusion in these cases, tapping the pericardial cavity would seem to be advisable. The demonstration of bloody fluid is helpful in diagnosis, the removal of the fluid may relieve the circulation. In certain cases it might do as much good as operation and might make operation unnecessary.

If signs of increased intrapericardial pressure develop suddenly, indicating rupture, the operation must be done without any delay. What one would expect to do at the operation would depend upon the conditions found. After the mediastinum is opened, the tamponade would be relieved by opening the pericardium. Procedures to start the heart beating may be necessary. If the heart is beating, the problem of preventing hemorrhage is presented. The methods of controlling hemorrhage will not be presented here.* Sutures should be placed at the site of the hemorrhage. If the myocardium is extensively bruised and softened, grafts of pericardium should be placed on the area of contusion and securely sutured to the myocardium. Adhesions between pericardium and myocardium is Nature's way of treating such contusions, but these adhesions may not give a secure union, and in our experiments they were absent in over half the cases. It is not a far stretch of the imagination to apply this operation not only to these traumatic cases but also to those cases in which myocardial infarction due to coronary disease is present. Such a graft placed over an infarct should afford protection from rupture.

CASES OF RUPTURE OF HEART RESULTING FROM NONPENETRATING WOUNDS OF CHEST

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MECHANISM OF PAIN PRODUCTION IN ANGINA PECTORIS*†

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INTRODUCTION

DURING the past few years we have investigated several aspects of the problem of pain production in angina pectoris. The work dealt in part with patients having angina pectoris, in part with the production of pain in contracting skeletal muscles in normal persons, and in part with animal experimentation. In this report an attempt is made to summarize briefly the various deductions and conclusions derived from the foregoing studies.

The subject of angina pectoris is an old one, and the theories concerning the mechanism of its production are manifold. At the present time, however, the majority of workers have come to view ischemia of the heart as the most likely cause for angina pectoris. There is no need of reviewing the pertinent literature in view of the several excellent reviews already published among which the more recent are those of Keefer and Resnik[1] and Lewis.[2]

The evidence for the ischemic theory of angina pectoris has been derived from four sources: (1) that based on clinicopathological correlations; (2) that based on clinico-electrocardiographic correlations; (3) that dealing with observations on contracting ischemic skeletal muscles; and (4) that dealing with observations made on animals.

CLINICOPATHOLOGICAL CORRELATIONS

While the commonest pathological lesions found in patients with angina pectoris are coronary sclerosis and myocardial fibrosis, these lesions of the heart often occur without being associated with angina pectoris. Even in coronary thrombosis the dramatic clinical picture is sometimes absent (cf. Saphir, Priest, Hamburger and Katz[3]). It is not difficult to explain the occurrence of pain in the foregoing conditions on the basis of relative or absolute ischemia of the heart. It is much more difficult to account for the absence of pain when a similar degree of ischemia is present, unless some other factor or factors are concerned.

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CLINICO-ELECTROCARDIOGRAPHIC CORRELATIONS

A similar conclusion was reached from an analysis of clinico-electrocardiographic studies. In confirmation of the work of others we have found that bodily exercise and generalized anoxemia may precipitate attacks of angina pectoris in patients suffering from this disease, usually with alterations in the electrocardiogram similar to those in spontaneous attacks of angina pectoris. Similar electrocardiographic changes were produced in normal persons by these procedures without causing precordial pain and such electrocardiographic changes were found in patients with a history of angina pectoris following anoxemia or exercise even when unaccompanied by attacks of angina pectoris (cf. Katz, Hamburger and Lev,[4] Katz, Hamburger and Schutz,[5] and Katz and Landt[6]). These results also indicate that some other factor besides ischemia plays an important rôle in the production of angina pectoris.

OBSERVATIONS ON ANIMALS

A clue to the possible factors involved was derived from our animal experiments. In the course of an investigation of the pathways taken by the pain fibers in the dog we had occasion to repeat some of the experiments of Sutton and Lueth[7] and were surprised to find that the responses recorded by these authors did not always occur (Katz, Mayne and Weinstein[8]). We were able to confirm the observations of previous workers that occlusion of the coronary vessels and the surrounding tissues in the unanesthetized dog gave rise to effective responses resembling an anginal attack. The response was similar to that obtained on compressing a superficial somatic sensory nerve except for the inability of the animal to locate the site of irritation. However, our results showed that the pain response was not due to the occlusion of the coronary artery but to stimulation of afferent pain fibers located in the nerve plexus surrounding the vessels. The evidence for this is:

(1) Occlusion of a carefully isolated strip of the coronary artery gave no response, but a definite response was obtained when the undissected coronary vessel was compressed above and below this point.

(2) Destruction of the nerve plexus surrounding the vessel with phenol-alcohol abolished the response to compression, but the response was still positive when a region above the phenolized area was stimulated.

(3) Complete preliminary occlusion of the carefully isolated coronary artery did not prevent a positive response to compression above or below this point.

(4) Pericardial "tamponade" following bleeding from a ruptured coronary artery caused syncope but no "anginal" response.

Positive responses occurred only when the region about the coronary vessels was compressed, the rest of the myocardium and epicardium

was found to be insensitive to pressure stimulation. As a result of this study it can be concluded that ischemia of the myocardium need be only one of many mechanisms operating on the nerve endings and nerve fibers surrounding the coronary vessels which can give rise to anginal attacks. It is conceivable that sudden rises in blood pressure could mechanically stimulate these nerve endings and give rise to pain attacks. Furthermore the direct action of the arteriosclerotic processes on the coronary vessels spreading to the adventitia and accompanied by periarterial changes could render the nerve endings within the walls at first hyperirritable and later, by destruction, insensitive to stimulation. Such changes would most certainly alter the pain response. Stimuli which would ordinarily be without effect on the pain endings might be effective when the nerve endings were hyperirritable. This may be the crux in the difference in response to the same stimulus in different patients. It must be further borne in mind that during the process of involvement of the nerve endings and also of the nerve fibers in the adventitia, the actual advance of this pathological process may by itself give rise to painful attacks as successive groups of fibers and endings are first stimulated and then destroyed. Myocardial infarction may operate in exactly this way on the nerve endings and nerve fibers present in the infarcted area.

It is not unlikely that the pain response obtained by Sutton and Lueth[7] in probing the mouths of the coronary vessels might have been due to stimulation of this nerve plexus rich in pain fibers and not directly to the occlusion of the mouths of the coronary arteries. It is indeed possible that even sudden death, the result of ventricular fibrillation, could have been caused by reflex or direct nerve stimulation.

OBSERVATIONS ON CONTRACTING SKELETAL MUSCLES IN NORMAL PERSONS

The greatest support for the ischemic theory has come out of the work on human skeletal muscle. It has been known for a long time that continuous pain can be produced in contracting skeletal muscle when the muscle is rendered ischemic. The concept that it is due to spasms of the vessels has been definitely disproved by the work of Lewis, Pickering and Rothschild.[9] The immediate factors responsible for the muscular pain have not been fully established. The pain which develops in contracting muscles during ischemia might be caused (1) by the direct or indirect action of the lack of oxygen which accompanies ischemia, (2) by the diminution of other materials normally supplied by the arterial blood, (3) by the incomplete mechanical removal of products of muscular metabolism which follows the retardation of the blood flow, or (4) by the combined action of several of these factors. The observations made in this laboratory on this phase may be sum-

marized as follows (Kissin,[10] Perlow, Markle and Katz,[11] and Katz, Landt and Lindner[12]).

(1) Generalized anoxemia, without impeding the circulation to a limb or obstructing its venous flow, lessens the amount of exercise necessary to cause continuous pain in the contracting muscles. The amount of exercise needed to cause pain decreases progressively but not linearly as the generalized anoxemia is augmented.

(2) Obstructing the venous flow in an otherwise normal limb also decreases the amount of exercise needed to cause pain, and in proportion to the degree of stagnation produced.

(3) When the circulation is free and anoxemia is absent, increasing the rate of exercise decreases the amount of exercise required to cause pain.

(4) A preliminary period of complete ischemia before starting the exercise definitely lessens the amount of exercise required to cause pain.

(5) Continuing the ischemia of the limb after stopping the exercise short of the point at which previous tests have shown that pain will appear, will lead to the appearance of pain after a long lag. This lag was found to be from 20 to 80 times longer than the time at which pain would have appeared if the exercise had been continued—which is roughly of the order of magnitude of the ratio generally accepted to exist between the metabolism of resting and exercising muscle.

(6) The condition of the limb before the exercise is started determines the amount of exercise required to produce pain, there is thus a definite pre-pain stage.

(7) Elevating the CO_2 content in the blood contained in an ischemic limb lessens the amount of exercise necessary to produce pain.

(8) Alkalinization of the subject by large quantities of sodium bicarbonate definitely increases the amount of exercise required to produce pain.

(9) We have confirmed the observations of Laplace and Crane[13] that fatigue, rather than unbearable pain, may, in some instances, make it impossible to further contract the muscles.

(10) We have obtained definite evidence that a substance formed during exercise of one group of muscles can pass the lungs and into another group of muscles, so that the amount of exercise required to cause pain is decreased in the latter.

From these observations we conclude that the stimulus for pain appears to consist of some metabolic product (or products) which is produced quantitatively in proportion to the work done by the heart. The amount of the chemical product produced for a given quantity of work is increased when the heart works inefficiently. Such inefficiency in cardiac work occurs especially when the diastolic blood pressure is elevated, because the heart has to exert more effort in raising the pressure of its contents above the diastolic aortic pressure

before it can expel the blood. This in part is also the cause for the inefficiency of the rapidly beating heat. A similar inefficiency occurs when the heart is failing, because the heart dilates in order to do its work.

The accumulation of the metabolic product which acts to stimulate pain is checked in part by a mechanical and in part by a chemical process. The first is a washing away of the substance by the circulating blood; the second is a local conversion to some other substance in the presence of oxygen. This pain producing substance will, therefore, increase in concentration whenever the circulation is slowed or whenever the oxygen content of the blood entering the coronary arteries is decreased.

Our work indicates that a pre-pain stage exists in which the metabolic product causing pain is increased in amount but not sufficiently to stimulate the pain end organs. As in the case of all sense organs, a certain threshold value must be reached before the end organs respond. In the pre-pain stage the concentration of the chemical product may vary within wide limits (from zero to the threshold value). This variability in concentration in the pre-pain stage is one of the reasons for our inability to predict whether or not a given set of circumstances will lead to a paroxysm of pain. It may explain in part why the factors required to cause pain are so variable in different patients and even in the same patient.

SUMMARY

In other words it would appear that the stimulus for pain is a metabolic metabolic product (or products) which can readily diffuse into the blood stream and which can be quickly altered in the presence of an adequate supply of oxygen. The accumulation of this product is dependent upon the amount and character of the physical work and the efficiency, on the one hand, and the quantity of the oxygen and blood supply on the other. When this substance reaches a concentration above the threshold of the pain end organs, pain results. This chemical product appears to be acid in character, or at least one that is additive with acid substances and is "neutralized" by alkaline substances. In all probability it is some substance like lactic acid or phosphoric acid formed during the catabolism of muscular activity.

Work remains yet to be done on many aspects of the problem of pain production, especially in accounting for the variations in pain responses under what seem to be similar conditions. An important factor responsible for this variability, it seems to us, is the inconstancy of the state of the pain receptors and pain pathways and the fluctuation in the sensorium for perception of pain sensation. Work on these phases is now in progress.

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PATHOLOGY OF CORONARY SCLEROSIS*

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COMPARATIVE study of a large series of coronary arteries from cases in which lesions of these vessels have been responsible for the fatal issue revealed histological differences which caused the cases to fall into two groups.† The first of these groups was found to include all of the younger members of the series with two exceptions. The second group included, with these exceptions, the older members of the series. The exceptions, on microscopical examination, were found to be secondary processes in coronary arteries in young men in which earlier thrombosis and repair had occurred, thus leading to conditions which produced lesions typical of the older group. The ages covered by the first group of fatal cases were from twenty-five to fifty-five years. The ages in the second group were from forty-seven years up to old age.

Microscopically the lesions of the first group were characterized by fibrosis and a minimal persistence of lipoid cells. Per contra the lesions of the second group were distinguished by the massing of lipoid cells and a relatively small amount of fibrosis. It became apparent that the differences in these two series were dependent upon a reaction to the presence of lipoid cells in youth which caused a stimulation of connective tissue that tended to replace the lipoid cells as they were deposited. In the older group this reaction was lacking and lipoid cell deposits became so excessive, with attendant poor nourishment, that massive necrosis and formation of atheromatous cavities became the standard picture before death.

Since the differences described appeared to center about variations in the phenomena associated with the appearance of lipoid cells in the lesions, resort was had to the study of the earliest lesions obtainable in an effort to determine the provenance of these lipoid cells and the evolution of the lesions which were associated with them.

Three sources proved helpful: first, examination of the finer branches of the coronary arteries in young individuals whose main trunks had undergone advanced processes; second, the routine study of sections of

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†It has been the custom to lay open the coronary arteries with so-called coronary scissors. The use of scissors disturbs the normal relations and has tended to confuse the issue. Coronary arteries should be examined grossly by serial cross-sections with a sharp knife.

coronary arteries in young individuals who had died from any cause; third, the study of sections of the coronary arteries from cases of congenital heart disease.

It is recognized that the coronary arteries undergo at least more unusual and probably greater stresses than do other muscular arteries. The stresses are greater because the coronary arteries originate at a point where the highest arterial pressures are found, i.e., at the aortic ring.

Fig. 1.

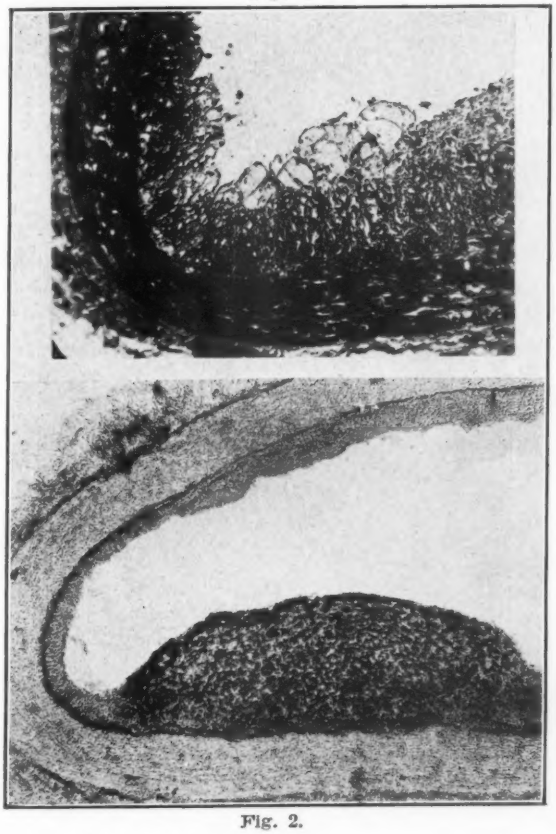

Fig. 2.

Fig. 1.—Left coronary branch. Lipoid cells.
Fig. 2.—Left coronary branch. Note the normal internal "buffer" layer lining vessel apart from the atherosclerotic nodule, from same lesion shown in Fig. 1, at a lower level. Fat stained with sudan IV.

It is generally agreed by physiologists that those portions of the coronary arteries which lie in the subepicardial tissues are subjected during systole to pressure from the blood within the aorta and resistance from their myocardial branches which are being compressed by the contracting heart muscle, so that during a part of the cardiac cycle the pressures in the larger coronary vessels are unusual. It is further probable that the curve which the left coronary takes in its proximal inch, from an

orifice at right angles to the aortic wall to a position paralleling that wall, causes this portion of the vessel to undergo great stress. The origin of a large branch, the circumflex, probably also influences the pressures within this region, which is the favorite locus for serious or fatal forms of coronary atherosclerosis. The formation of a buffer layer of unstriped muscle and fibrous tissue in the subendothelial layer of the intima of the coronary arteries, and notably in the proximal portion of

Fig. 3.

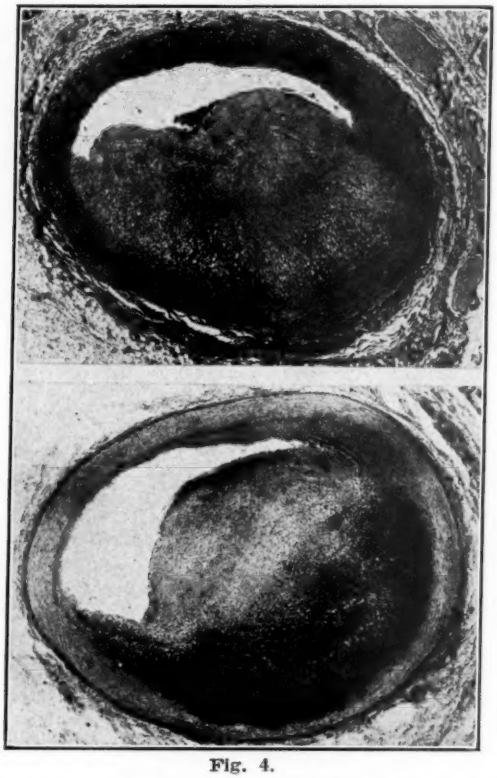

Fig. 4.

Fig. 3.—Left coronary artery. Fibrosis near lumen—lipoid cells in depths.
Fig. 4.—Left coronary artery, from same lesion as Fig. 3. Fat stained with sudan IV.

the left coronary artery, as a standard finding in these vessels, even in early youth, is probably due to the great and unusual stresses which these vessels undergo.

The study of the left coronary artery in cases of congenital heart disease was fruitful, since unusual stresses were to be expected in the effort to overcome the developmental faults in the organ. The earliest atherosclerotic processes were found in the left coronary arteries of hearts with congenital disease.

Early stages in the progressive changes in the coronary artery of a young individual are well shown in the case of M. R., from whose left coronary the sections illustrated in Figs. 1 to 4 were obtained. A boy, eighteen years old at the time of his death, had a traumatized hip when seven years of age, followed by tubercular disease. He was treated through the following years but healing was accompanied by fixation of the hip joint. One year before his death he developed pleuritis with effusion, which subsided. Following a plastic operation to relieve the deformity of the hip, wound infection leading to streptococcus septicemia caused his death. The heart was submitted for routine coronary examination through the courtesy of Dr. Frederic Parker, Jr., by Dr. Edward Hayes. In Fig. 1 is seen the earliest lesion, a collection of lipoid cells beneath the intima of a branch of the left coronary artery. Fig. 2 is from a frozen section at almost the same location and is stained with sudan IV. The largest masses of the lipoids occur beneath the surface endothelium where they lie in large macrophages which are of recent origin. The lipoid cells which have migrated more deeply are smaller, and therefore the lipoid masses are smaller in the depths. Fig. 3 is from a section of the main left coronary artery above the orifice of the circumflex branch, which came off at a low level. The more advanced intimal process is marked by fibrosis of the inner layer, and spaces appear in the deep layer representing lipoid cells which had migrated more deeply as fibrosis progressed internally. A frozen section from the same location (Fig. 4), stained with sudan IV, reveals the lipoids now placed deeply beneath the inner fibrous layer, including some invasion of the media.

Beginning with these early lesions and proceeding through older processes to the late fatal lesions one can reconstruct the stages in the development of a disease, the beginnings of which may be found in the earliest days of life.

The earliest phenomenon is the deposit of free lipoid beneath the endothelium of arteries, i.e., lipoidosis. That stresses favor this deposit is suggested from the sites in which lipoid material occurs in the aorta, in which vessel they are most readily seen and have been most extensively studied. The deposit is evidently bland and does not provoke a fibrous reaction even in the very young.

The next step is the appearance of phagocytic cells which engulf the lipoid. The origin of these cells is still undetermined. They are not histiocytes, i.e., wandering connective tissue cells which have been resting in the tissue interstices. When these cells engulf and remove blood from a clot, for example, they can be seen throughout the tissues in the neighborhood of the clot. Nothing resembling this picture is seen in either human or experimental atherosclerosis. The cells may be monocytes which invade the regions where lipoid is being deposited or perhaps in some cases carry the lipoid into the regions where they come to rest.

Study of both experimental and human lesions makes me lean toward a belief that these cells arise locally from the subendothelial connective tissue.

The occurrence of lipoid cells is progressive in most cases, new cells replacing the old in the surface layer as the old migrate to a deeper position or are replaced by fibrous tissue. In some cases they apparently

Fig. 5.

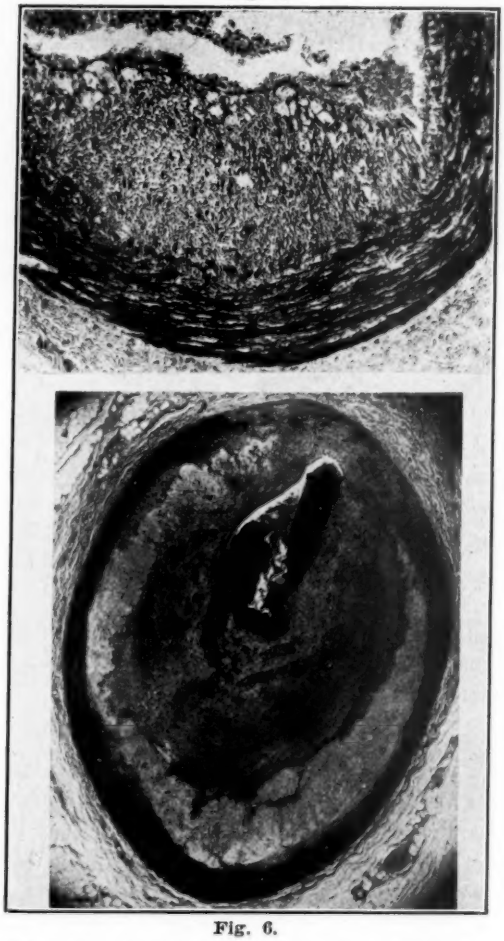

Fig. 6.

Fig. 5.—Early diffuse fibrosis developing in an early lesion of a small left coronary branch in a man of twenty-eight years, whose death was due to thrombosis of the left coronary artery, descending branch, beginning 1.5 cm. from orifice.

Fig. 6.—Typical fibrotic lesion with thrombosis in the descending branch of the left coronary artery of a man twenty-six years of age—eccentric fibrosis, nutritional necrosis of the layer farthest away from the lumen; acute fibrinous necrosis, terminal, near lumen. Note hypertrophy of media.

arise cyclically as indicated by the deposit of lipoid cells and fibrous connective tissue in layers. The presence of lipoid cells in the intima of the young, rabbit or man, is followed by a growth of fibrous tissue.

There is a suggestion that metabolism of the lipoids within the cells is responsible for the stimulating effect upon the neighboring connective tissue. Free lipoid, in lipoidosis, does not have this effect. Fibrosis may be a focal process arising in the depths of the subendothelial tissue and progressively replacing the lipoid cells, abolishing them as it spreads. More frequently it is a diffuse process, the reticular strands between the lipoid cells increasing in thickness in the young as the cells decrease in size until finally the cells disappear (Fig. 5).

The nutrition of the newly formed fibrous tissue is dependent upon imbibition from the lumen. As the fibrotic layer increases in thickness, the nutrition of those portions which are most distant from the lumen tends to suffer. The lesions are usually eccentric, the narrowed lumen dislocated to one side (Fig. 6). In advanced lesions it is usual to find a crescentic region of necrosis of those portions of the intimal tissue most distant from the lumen, i.e., next to the media. The necrosis of the intimal tissue tends to be preceded or accompanied by a deposit of fat either in droplets or more diffusely along the broad collagen bands which often make up the deeper layers. This secondary fat deposit is probably related to degenerative changes in the fibrous tissue preceding necrosis. Lymphoid cell infiltration, absent from the early stages, tends to occur at this time.

The fatal issue most frequently arises as the result of a new and different type of necrosis, fibrinous or fibrinoid, arising focally in the fibrous tissue near the lumen and extending to the endothelial layer. Endothelial necrosis is followed by thrombosis. Or death may be due to inadequacy of the circulation through the narrowed lumen under conditions of stress without thrombosis. The more significant strains on the cardiac functions which tend to lead to fatal terminations are, in the order of their importance, indigestion, physical or psychic stress, and exposure to cold.

So much for the picture in youth. In older human beings the same appearance of lipoid cells provokes no fibrosis. As new cells arise the older cells migrate or are forced to a deeper position, and ultimately large collections of these cells are found. Their nutrition is hazardous, depending as it does on imbibition, either from the lumen or sometimes from vasa vasorum. There is no true vascularization of the cell masses. The cells occur in spaces in a delicate linear reticulum either singly or in small groups in each space. Necrosis, usually massive, is the standard outcome. The lipoids are freed from the cells. According to the studies of Kimmelstiel[1] the lipoid esters making up the contents of these atheromatous foci are mixtures of esters of cholesterol, phosphatides and cerebrosides. Cholesterol is a relatively insoluble hydrophobic colloid. Mixtures of its esters with those of other lipoids, which tend to form hydrophilic emulsions, increase the solubility of the cholesterol. When extensive necrosis of lipoid cells occurs, the more soluble lipoids appear

to be largely absorbed from the mixture, leaving the relatively insoluble cholesterol, which crystallizes out. An atheromatous cavity may contain, therefore, some living lipoid cells, cell detritus and crystals of cholesterol, together with fluid which may include lipoid esters or free lipoid.

The formation of an atheromatous cyst, cavity or "abscess," as it used to be called, presents a new hazard. Located in the intima of a muscular artery which is constantly undergoing dilatation and contraction is a cavity filled with semifluid material. Rupture of an atheromatous abscess in the aorta is attended with no considerable danger. The contents are broken up in the rapidly moving stream and the fine solid fragments diffused widely. In the coronary artery, rupture usually leads to obstruction of the lumen of the vessel near the point of rupture (Fig. 7) or to complete plugging of branches. The material is not broken up, but acts as a semisolid mass. In most cases death is sudden, but time

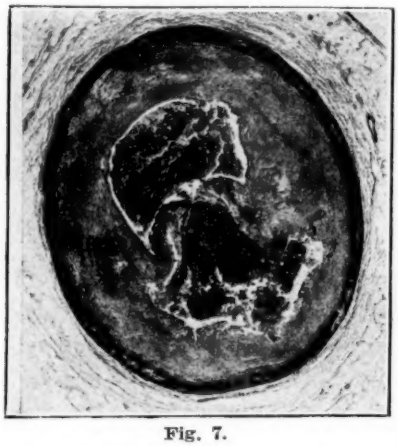

Fig. 7.

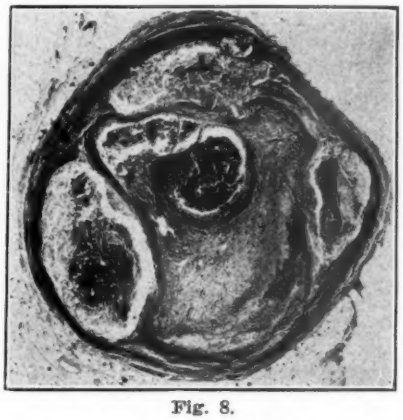

Fig. 8.

Fig. 7.—Point of rupture of atheromatous "abscess" in a man sixty-six years of age. Descending branch of left coronary artery 2 cm. from orifice. Lumen to the left and above filled with contents of "abscess." The vessel below this level contained clot and "abscess" contents.

Fig. 8.—Section of left coronary artery of a man sixty-two years of age. There are four atheromatous "abscesses." The central lumen is filled with clot and "abscess" contents. Probable rupture of the atheromatous focus nearest lumen.

enough has usually elapsed before the death to permit of clotting, either platelet or mixed clots arising (Fig. 8). As in the young, death may occur from coronary insufficiency, under stress, without rupture of an atheromatous cavity or thrombosis.

Mucoid changes in the later stages of atherosclerotic processes are not uncommon. They have the character of secondary degenerative processes and are met with usually in the intima but also in the media. In my experience so-called mucoid degenerated tissue is the substratum left in celloidin or paraffin sections after extracting lipoids by the fat solvents used in preparing tissue for paraffin or celloidin imbedding. In frozen

sections the lesions show free lipoids in the loci found in paraffin sections which exhibit mucoid changes.

Jenner's famous letter to Parry reporting calcification of the coronary arteries in the first case described in England, shortly following Heberden's coinage of the term "angina pectoris," has led most clinicians to look upon calcification of the coronary arteries as common and important. Calcification of the coronary arteries is a much later manifestation and less common than is calcification in the aorta. The deposit of lime salts in tissues is always an end-result, of monumental character, marking the site formerly occupied by living tissue. From any standpoint calcification is of no importance in the etiology of the lesions and is only significant in that a coronary vessel converted into a rigid tube is no longer subject to the influence of spasm of the media, though on the other hand it is no longer capable of dilating.

COMMENT

The lesions of atherosclerosis have been found in this series as early as the third day of life in the left coronary artery of a case of congenital heart disease (pulmonary and tricuspid atresia, cor triloculare). The lesions are not rare in coronaries of the first decade of life and are more common in the second decade. Fatal coronary thrombosis is found in the third decade and is relatively common in the decades which follow.

One can conclude therefore that atherosclerosis is a disease and not the inevitable consequence of age.

Study of the early lesions of atherosclerosis demonstrates that inflammatory elements are lacking. The lymphoid cell infiltration met with in the late stages is usually associated with secondary necrosis arising in the thickened intima, or appears in connection with terminal infections. The disease is therefore not inflammatory in origin.

The distinctions between the lesions of youth and old age are dependent upon a reacting ability in youth which results in fibrosis and upon a lack of this reaction in age.

Early lesions are always intimal with secondary effects on the other layers of the vessel wall. Though stresses are probably causative factors, morphological evidence of damage to the elastica is usually a secondary phenomenon. The media is more often hypertrophied, either locally or generally, than not. Evidence of other pathological change in the media is also secondary.

The lesions of atherosclerosis center about the deposit of lipoid cells in the intima. One can conclude that this disease with its intimate relation to lipoid cells is probably metabolic and results from the failure of a metabolism having to do with lipoids. Is there such a metabolism? Cholesterol is a lipoid which is found in nature only in animal bodies

and their products. We think of it in terms of blood and bile cholesterol. We forget that cholesterol is the basic substance of every animal cell. Starling looks upon it as the stable material of the animal cell, relatively insoluble and fixed, serving as the framework, so to speak, of the cell, in the interstices of which the more labile substances undergo their metabolism. All of the human supply of cholesterol is derived from ingestion. None is synthesized, as far as is known. The herbivora synthesize cholesterol, possibly from the closely allied phytosterols, which have the same formula as cholesterol, but a different molecular arrangement. The cell needs for cholesterol are greatest in times of rapid cell division. Egg yolk rich in cholesterol is intended for the embryo. Milk, the fats of which contain cholesterol, is intended for the infant. The increase in blood cholesterol in pregnancy is a mobilization of this substance for the needs of the fetus in utero.

Man is the only animal that ingests eggs and milk throughout its lifetime. Man is also the only animal, as far as is known, that dies in early life of coronary sclerosis, and suffers almost universally from atherosclerosis in the later years of life.

Finally it is possible to reproduce the lesions of human atherosclerosis in the rabbit, by the feeding of cholesterol. Moreover human dietary experience in diabetic individuals supports the results of rabbit experimentation. Under excessively fat diets rich in cholesterol, atherosclerosis increased at such a rate as to focus attention, xanthomas were common, and atherosclerotic calcification of the leg arteries of children could be demonstrated by roentgen examination. Recent reports from the Joslin clinic indicate that under a lowered fat diet atherosclerosis is less outstanding, xanthomas no longer occur, and evidence of calcification of leg arteries in children is lacking.

Atherosclerosis has close analogies with that other important metabolic disease, diabetes. In both rabbits and man variations in idiosyncrasy to cholesterol are evident. As in diabetes the inheritance of a poor cholesterol metabolism may result in early manifestation of disease in the form of coronary sclerosis. As in diabetes the loss of efficiency of the metabolic machinery with age results in more frequent late manifestations of the disease. As in diabetes the secretion of a ductless gland appears to control the metabolism. Thyroid feeding is apparently capable of preventing the production of experimental atherosclerosis in the rabbit.

It has been observed for many years that arteriosclerosis was related to the inheritance of a familial diathesis or disposition which might manifest itself in the form of diabetes, gout, or obesity. As one glances at the group it is apparent that these are all disturbances of metabolism. The demonstration that atherosclerosis, the most important form of arteriosclerosis, is a metabolic disease, fits it appropriately into this group.

SUMMARY

From this study of the lesions of coronary sclerosis it is evident that the pathology of the disease as described in most textbooks needs to be rewritten. The descriptions of the pathology in these works have been based on cases of coronary sclerosis in which the patients have been hospitalized and in which secondary changes, including infarction with associated inflammatory reactions, have tended to obscure the picture. The material for this investigation has come from early lesions or from patients who have literally "dropped dead." This has permitted of the study of the primary process uncomplicated by secondary reactions.

These studies demonstrate that the standard lesion in coronary sclerosis is atherosclerosis; that the lesions arise from the entrance of lipoids into the subendothelial layer of the intima and their phagocytosis by cells referred to herein as lipoid cells. In the young the presence of these lipoid cells stimulates growth of fibrous tissue. As a result, the standard picture in coronary disease in the young is fibrosis, narrowing the lumen of the artery. Death is usually due to thrombosis. In the old the presence of lipoid cells does not stimulate fibrosis. The cells accumulate in large masses, the nutrition of which becomes inadequate. Necrosis and autolysis result in liquefaction of the cell masses, and atheromatous "abscesses" result. Death is usually due to the rupture of an atheromatous "abscess" into the lumen.

It is possible to reproduce the lesions of coronary sclerosis in experimental animals by feeding the lipoid, cholesterol, which makes up most of the lipoid contents of atherosclerotic lesions.[2] The lesions, natural and experimental, are primarily intimal and lipoid. Lesions of the elastica and media are secondary. Inflammatory reactions are late phenomena following necrosis and are not an essential part of the picture.

Atherosclerosis is a disease due to disturbances in the cholesterol metabolism and belongs with the other metabolic diseases, diabetes (carbohydrates), gout (purines), and obesity (fats).

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CORONARY SPASM AS A POSSIBLE FACTOR IN PRODUCING SUDDEN DEATH*

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INTRODUCTION

"IN MEDICAL observations it is not always possible to get direct evidence for the solution of a problem. We then have to proceed by inference."[1]

Though many theories have been advanced to account for the pain in angina pectoris, the medical world in general has come to accept Mackenzie's thesis that the pain is of cardiac muscle origin, and is due to an inadequate supply of blood, leading to muscular exhaustion. The pain may be produced by overwork even when the blood supply is normal. It usually comes on during stress conditions, but also may come on hours after the effort which led to a muscle strain approaching exhaustion. In any case it depends upon the blood supply to the organ. A normal supply may be inadequate under conditions of great stress. A diminished supply may be inadequate under conditions of minor stress. The degree of pain which the individual suffers will depend upon the degree of inadequacy of the blood supply under the conditions obtaining, and upon the sensibility of his nervous system.

Attacks of what Mackenzie calls secondary angina pectoris may arise in individuals with a widespread hypersensitiveness of the nervous system. The attacks of angina in this group subside following removal of the cause of the nervous hypersensitiveness. As Mackenzie indicates, the primary cause is not cardiac, therefore the angina is secondary in character. This concept almost requires the deduction that under hypersensitive reflex excitability the blood supply to the heart muscle, in order to produce the pain, becomes inadequate during the attacks. The only reasonable manner of causing this inadequacy is by contraction of the coronary arteries under nervous control, thus limiting the blood supply. That the blood supply is adequate between the attacks is evidence that the quality of the blood is not the important factor, and that the heart muscle is not in a permanently exhausted state. The disappearance of all symptoms following cure of the local condition, in some other part of the body, which was responsible for the widespread hypersensitiveness of the nervous system, can be accepted as fairly good evidence that

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the cardiac circulation was unimpaired following the period of anginal attacks. All of this points to coronary artery spasm as the source of the attacks.

THE CONDITION OF THE MEDIA IN CORONARY ATHEROSCLEROSIS

Atherosclerosis of the coronary arteries is a primary intimal process in which the media may remain almost intact even in moderately advanced cases. Invasion of the media by lipoids or lipoid cells or by extension of the fibrous tissue from the intimal lesion is a secondary phenomenon. The media may indeed show general or focal hypertrophy. Atrophy, apart from that arising from extension of the intimal lesion, is not general or striking, except as a late phenomenon. The possibility

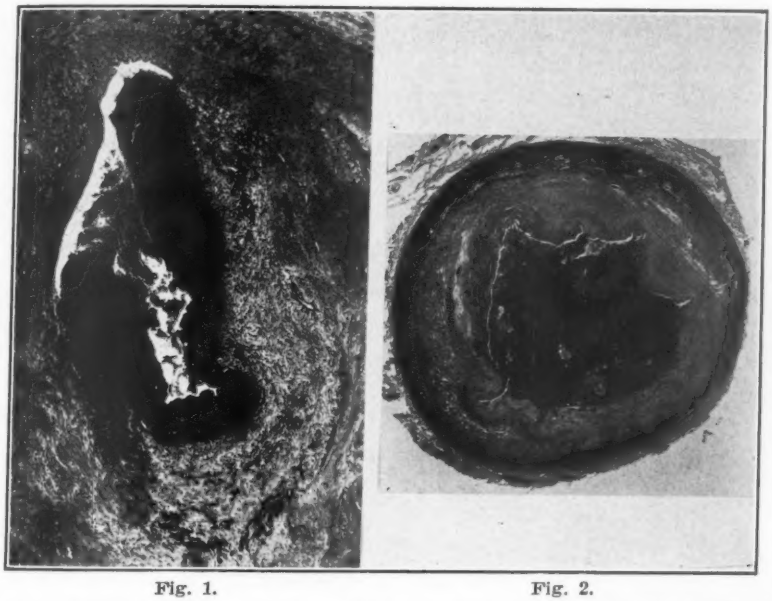

Fig. 1. Fig. 2.

Fig. 1.—Coronary artery. H. W. T., male, twenty-six years old. Lumen with thrombus. Fibrinous subendothelial necrosis arising below lumen and extending to the endothelium on the left.

Fig. 2.—Coronary artery with thrombus. J. J. K., male, thirty-seven years old. Note angulation of lumen and hypertrophy of media.

that muscular spasm may exert a compressing force on the intimal lesion is therefore existent in most coronary vessels, excepting perhaps in advanced old lesions in which tubelike deposits of lime salts have made the walls rigid.

That spasm may be a factor leading to the fatal issue is suggested by:

I. MORPHOLOGICAL EVIDENCE

a. *Coronary Thrombosis.* In about 75 per cent of the cases showing fibrosis with narrowing of the coronary lumen, occurring in the young, there is found an acute type of fibrinous or fibrinoid necrosis appearing

in the subendothelial connective tissue and extending to the endothelium (Fig. 1). This type of necrosis, arising near the lumen, and therefore in well-nourished tissue, is in contrast to the slower nutritional type of necrosis arising in those portions of the intimal fibrous tissue most remote from the lumen, i.e., near the media.

The constant natural traumatisms to which the endothelium lining vessels in the hands, feet, buttocks, and back must be subjected without harmful result indicate a high resistance of this tissue to violence. The indignities to which this layer may be subjected without damage in connection with certain operative procedures in which tissues are temporarily clamped tend also to establish the hardiness of this layer. On the other hand, the foreign fibrous tissue which is formed in the sub-

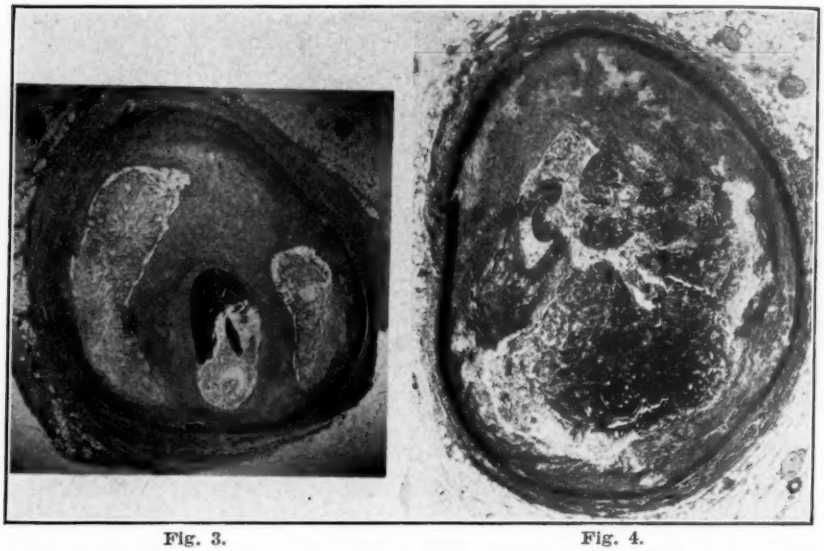

Fig. 3. Fig. 4.

Fig. 3.—Coronary artery. J. K., male, sixty-six years old. Atheromatous "abcesses" on either side of lumen. Atheromatous material in lower part of lumen. Thrombus with atheromatous material above.

Fig. 4.—Coronary artery. N. P., male, sixty-six years old. Rupture of atheromatous "abscess" below into narrowed lumen above. Note wide tearing of tissues.

endothelial layer of the intima in atherosclerosis is less well nourished and might well be injured by spasm of the media, while the endothelium lining the vessel is unharmed. Even though the endothelium is damaged, it is still able to function until some more efficient destructive agency comes into action. Extension of necrosis from the subendothelial tissues to the endothelium may supply this more efficient agency. Endothelial necrosis leads to thrombosis.

The angulation of the lumen found not rarely in the coronary arteries of young persons with fibrotic intimal thickening suggests an increased muscle tonus, notably when the media is hypertrophied. This picture depends in part upon connective tissue rigidity and redundancy when the vessel is contracted, but the contracting force is the muscle (Fig. 2).

b. *Coronary Obstruction by Rupture of Atheromatous "Abscess" Contents.* Rupture of an atheromatous cavity into the lumen or the rare reverse process, rupture from the lumen into the cavity, is the standard terminal lesion in older persons. It is possible that thinning of the membranous partition, which comes to be the only barrier between the cavity and the lumen, may lead by its own weakness to rupture, placed as it is in a muscular vessel. If this were true in general, the lesion should be marked by the filling of the cavity with blood, during systole, washing out the contents. Ordinarily the cavity is found more or less empty, indicating delivery of its contents by positive pressure. That rupture is not an artefact produced by the handling of the vessel post mortem is

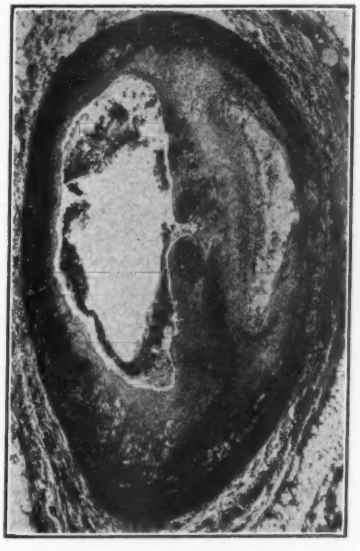

Fig. 5.—Coronary artery. G. H., male, thirty-eight years old. Note hypertrophy of media. The pale foci extending into media below were occupied by lipoid. Section from point of greatest narrowing.

evidenced by the diffusion of atheromatous material through thrombi. Atheromatous material is not readily mixed with blood, notably clotted blood (Fig. 3).

The character of the tear in the limiting membrane and the endothelial lining of the vessel tends in many cases to negative the hypothesis of more or less passive rupture. Oftentimes the rupture is associated with splitting of the separating layer, not a mere tearing through. It is true that in some cases necrosis at the site of rupture has preceded the breach in the wall, but this is exceptional. Compression of the cavity contents and their forceful delivery through the rent in the wall best account for the appearances found (Fig. 4).

c. *Coronary Insufficiency*—with spasm? The following case is typical of a condition which suggests the possible influence of spasm.

G. H., an Armenian, thirty-eight years of age, 5 feet 6½ inches in height, body weight 156 pounds but with very fat abdomen, had always been in good health. His wife stated that he had never consulted a doctor, and had not suffered from indigestion. On the day of his death he accompanied his son, twelve years old, to a conservatory of music. The boy had been taking lessons on the violin, and the father was for the first time to be present during his son's lesson. Furthermore the teacher would play a duet with the boy. The father was much stirred emotionally in expectation of an experience to which he had looked forward. He collapsed in the office of the conservatory, was brought to a hospital, and pronounced dead on arrival. The indications were that death had occurred almost immediately after his collapse. The heart weighed 350 grams, with some left ventricular hypertrophy. The valves and cavities were normal. There were yellow opaque patches in the aortic arch about the ring, with slight narrowing of the orifice of the left ocoronary artery. The walls of the coronary arteries were thickened, for the most part moderately. Gross section of the left coronary disclosed longitudinal ridges in the inner layer, suggesting wrinkling of the thickened intima. There was no thrombosis. Microscopical examination of the left coronary artery revealed fibrosis of the inner layer of the thickened intima, abundant lipoid cells more deeply placed and focal lipoidosis of the media. The lipoid in these medial deposits merely mechanically separated the muscle fibers, without evidence of any reaction. The media was definitely hypertrophied (Fig. 5).

The narrowing of the lumen of the vessels by the atherosclerotic intimal lesions was not adequate, of and by itself, to account for the death. The peculiar longitudinal folding of the thickened intima suggested an increased tonus of the hypertrophied muscle layer consistent with a concept that coronary spasm had been a factor in producing the sudden death.

II. ANGINAL ATTACKS FOLLOWED BY SUDDEN DEATH

a. *With Normal Coronary Arteries.*

V. I., a Lithuanian, twenty-three years of age, was an agent in a gambling number game. His father had dropped dead when forty-five years old. The son had had attacks of chest pain lasting several minutes during which he "could not lift" his left arm. The last attack occurred one month prior to his death. March 8, 1934, he had been drinking, came in to meet his employers, and was excoriated verbally and told to go home. He entered a bus, collapsed in the bus, could not be roused, and was removed in an emergency ambulance to a hospital where he was pronounced dead. Post-mortem examination revealed a heart weighing 340 grams, with slight left ventricular hypertrophy. The valves and cavities were normal. The coronary arteries were grossly normal throughout. The arch of the aorta was thin with a few pinhead yellow opaque foci. The aorta was thin, smooth, and elastic, with delicate yellow streaks along the line of intercostal orifices and about the orifices of abdominal branches. The pia-arachnoid was moderately injected and contained a moderate amount of clear serous fluid. The stomach contents, 400 c.c. of a yellow paste, had a strong odor of beer.

Microscopically the coronary arteries were lined by a "buffer" layer of unstriped muscle and fibrous connective tissue (Fig. 6), perhaps somewhat thicker than normal (Fig. 7). There was no evidence of atherosclerosis at any point.

No adequate cause of death was found at post-mortem examination in this case. The degree of alcoholism was not great enough to kill, and was particularly not adequate to kill suddenly. Chemical examination of

the stomach contents revealed no evidence of a poisonous agent. The history of a father who dropped dead, the personal history of attacks which were anginal in character, and the suddenness of the death following a scolding with threats of discharge, suggest that coronary spasm may well have been the cause of the attacks, and that the terminal one led to the death.

b. *With Minute Atherosclerotic Lesions.*

B. E. L., male, forty years of age, single. This man was an overseas veteran who had suffered attacks of angina over a period of years. He claimed that these were a sequence of his war exposure. The Veterans Bureau discredited his claims on the ground that he was a malingerer. He had had an attack of distress in the chest two weeks before his death. He did not sleep well on the night before his death because of discomfort in his chest and did not go to work in the morning. He went out at 9 A.M., returned in twenty minutes. At 11 A.M he again had acute

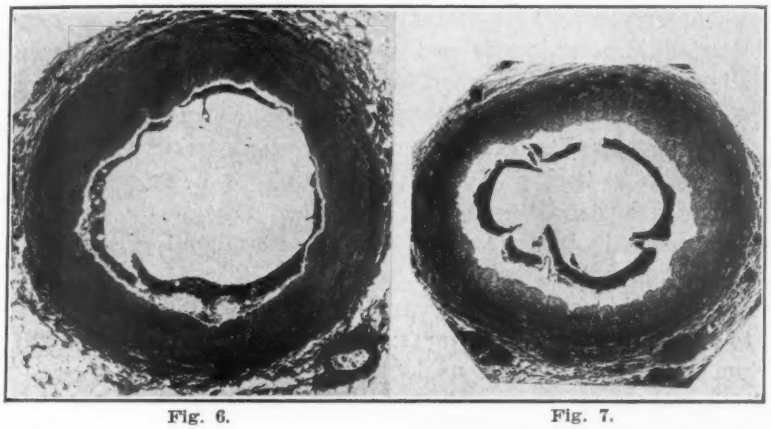

Fig. 6. Fig. 7.

Fig. 6.—Coronary artery. V. I., male, twenty-three years old. Somewhat thickened "buffer" layer lining vessel. Hypertrophy of media.

Fig. 7.—Coronary artery. M. R., male, fourteen years old. Normal coronary with "buffer" layer, somewhat thicker than average but within normal limits—for comparison with Fig. 6.

pain in the upper chest. A physician was called, who found him undergoing an attack of angina. He had drunk some peppermint, and was given ¼ gr. morphine in tablet form. Shortly afterward he was heard breathing heavily, had vomited and died suddenly at 1:30 P.M. Post-mortem examination disclosed a heart of normal size, the valves and cavities of which were normal. The muscle was homogeneous. The aorta was thin, smooth, and elastic. In the coronary arteries were found rare minute yellow foci, but the lumina were free, though vessels were of small caliber. The other organs were normal save for mild edema of the brain.

Death in this case demonstrated that the man was not a malingerer. A malingerer may appear to put one foot in the grave, but is careful to remove it before dangerous consequences arise. Again, in this case no adequate cause of death was found. The anginal attack seen by the physician preceding the death was of typical character and the presumption is that the previous attacks in which he was unattended

medically were similar. The amount of atherosclerosis of the coronary arteries was so slight that it might have been overlooked except for a thorough search.

COMMENT

The clinical and pathological material here presented can be, of course, only suggestive as to the possible rôle of coronary spasm in leading to attacks of angina or in producing sudden death. Frequently one sees cases of sudden death, particularly in hypertensive heart disease, in which post-mortem examination discloses coronary sclerosis without thrombosis, and with lumina of the coronary arteries large enough apparently to supply the needs of the heart muscle. The acute anginal attack or the death has occurred under physical or psychic stress, or accompanying indigestion or exposure to cold, or following these experiences. In many cases death occurs during the night while the patient is asleep. Asphyxiation by position while lying on the face or with the head buried in a pillow is met with almost wholly in epileptic or alcoholic persons. Other human beings who lie in dangerous positions escape asphyxiation by being wakened, the awakening usually coming following a nightmare. After such an awakening the individual comes to with a feeling of relief, as though he had been through a stressful experience. It is my belief that coronary deaths during sleep may be associated with the stresses which accompany nightmares.

One can understand how an acute need for blood under stress in hearts with rigid narrowed coronary lumina, due to calcification, could lead to anoxemia of the heart muscle and a resulting fatal issue. When the lumen is adequate and unobstructed in a still elastic vessel, the possibility that narrowing of the lumen by spasm under stress is responsible for the anoxemia presents the most reasonable explanation of the phenomena observed.

REFERENCE

1. Mackenzie, J.: Angina Pectoris, London, 1923, p. 40, Henry Frowde and Hodder & Stoughton.

INVERSION OF THE T-WAVE IN LEAD I OR II OF THE ELECTROCARDIOGRAM IN YOUNG INDIVIDUALS WITH NEUROCIRCULATORY ASTHENIA, WITH THYROTOXICOSIS, IN RELATION TO CERTAIN INFECTIONS, AND FOLLOWING PAROXYSMAL VENTRICULAR TACHYCARDIA*

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INTRODUCTION

IN THE course of routine electrocardiography our attention has been drawn occasionally to inversion of T in Leads I or II of the electrocardiogram in individuals who have shown no clear evidence otherwise of heart disease. Because inversion of T has been closely associated, and correctly, with serious myocardial disease, any exceptions deserve attention. Some of these exceptions are well known; some others, less commonly recognized, are herewith reviewed together with observations on neurocirculatory asthenia, a syndrome in which significant inversion of T has not been reported heretofore.

SELECTION OF CASES

Criteria designed rigidly to exclude patients in whom there existed some known causes for an inverted T, other than those under consideration, governed the choice of cases. Only patients in the younger age group were included. The history, physical examination, roentgenological and laboratory data were used to avoid instances of organic heart disease which are well known to cause inversion of T, namely, such affections as coronary disease, acute rheumatic infection, and acute or chronic pericarditis, and the inverted T associated with marked ventricular hypertrophy or intraventricular block. None of these patients was taking drugs of the digitalis series; none was suffering from myxedema, chronic nephritis, or drug intoxication. Each patient was reexamined at least once, and most were examined repeatedly over a period of months or years.

For greater convenience the patients in this series have been appropriately grouped, and each group will be considered separately. The case histories appended make an extensive discussion of the symptomatology unnecessary.†

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†The case reports upon which this study is based will be published in the reprints of this article.

NEUROCIRCULATORY ASTHENIA

This group comprises 7 patients, 3 males and 4 females, with an average age of twenty-four and one-half years. In not a single case was organic disease of any description found on repeated examination. In one patient an additional diagnosis was made of probable paroxysmal tachycardia; there was a history of a single attack lasting for five minutes five months before our examination. In one other patient an additional diagnosis was made of an anomalous electrocardiogram, consisting of a short P-R interval and wide QRS wave as reported by Wolff, Parkinson and White[1] in normal young persons.

The chief subjective symptoms were similar in each patient and were induced by abnormally small effort. Of the 7 in this group, all complained of palpitation, 6 were easily fatigued, 5 complained of dyspnea, and 5 suffered pain or ache in the region of the heart. All but two complained of "nervousness"; dizziness, faintness, and excessive sweating were less common complaints.

The heart size, measured from orthodiagram or teleroentgenogram, was not abnormal in a single instance. Heart rates were uniformly rapid and averaged 112 (limits 95 and 130) in the initial electrocardiograms. In 4 patients no murmurs were heard; in 3 an inconsequential systolic murmur was detected. The blood pressures of all were normal, as were the Wassermann and basal metabolic rate determinations when these tests were carried out. Other routine or special laboratory tests revealed nothing abnormal. As all the patients were reexamined at a later date, the possibility of overlooking incipient disease was practically eliminated.

At the time of the initial examination the electrocardiogram in each instance showed an upright T in Lead I and an inverted T in Leads II and III. No other important electrocardiographic abnormalities were found.

At the time of the last examination one patient was entirely well; five showed improvement of greater or lesser degree; while one remained unchanged. None had developed organic disease of any system; the clinical heart findings were not significantly altered except for the slower heart rates. Final electrocardiograms showed an upright T in Leads I and II and inverted T in Lead III in each instance. This change to upright T in Lead II was not associated with significant changes in the P or QRS waves. The heart rates, measured from the electrocardiograms, varied from 75 to 100, and the average was now 88.

Comment.—We have no good explanation for the significant inversion of T in the electrocardiograms of these patients. It hardly seems likely that the unknown mechanism behind neurocirculatory asthenia alone is responsible because this association is rare. There was neither

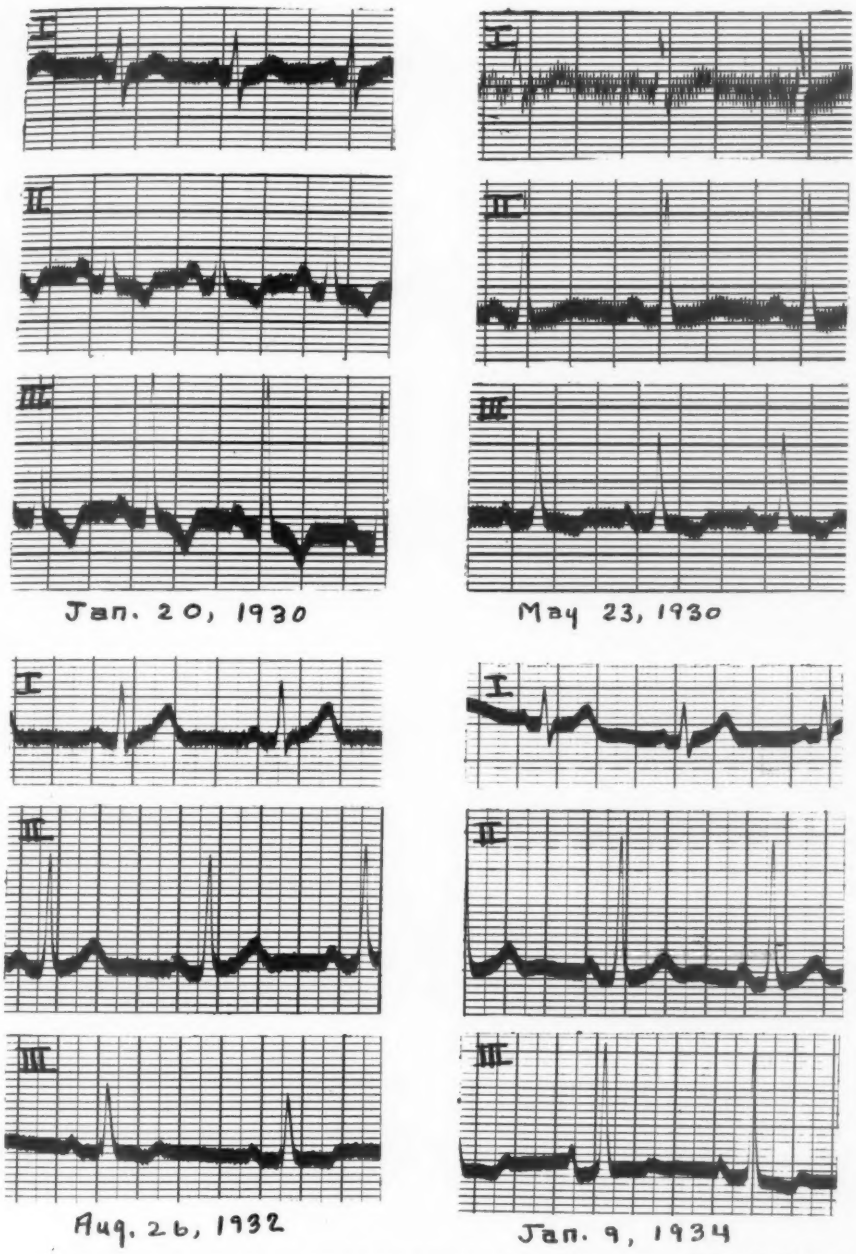

Fig. 1.—Electrocardiograms from Case 1 (boy aged fourteen years; neurocirculatory asthenia). January 20, 1930; showing inversion of T in Leads II and III. May 23, 1930; T in Lead II now upright but rather low. August 26, 1932, and January 9, 1934; T in Lead II normal.

recognizable inadequacy of the coronary circulation nor any other factor known to cause inversion of T.

Although a very occasional finding, inversion of the T in neurocirculatory asthenia retains importance because of the serious diagnostic error to which it may lead. A number of similar cases, in which there was strong evidence that important organic disease did not exist, we have not included because of their greater age or because of their failure to return for reexamination.

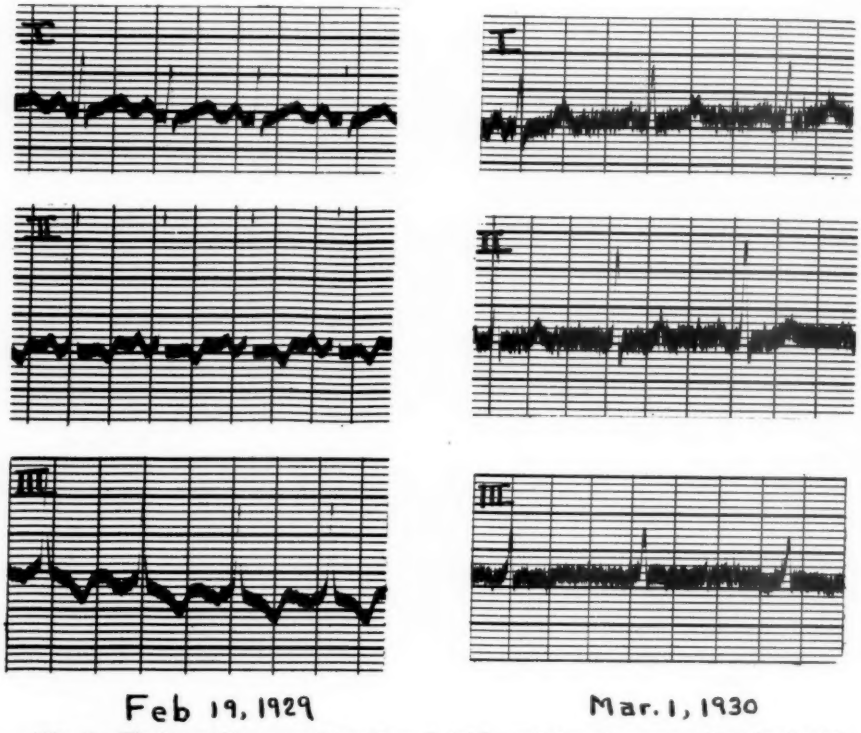

Fig. 2.—Electrocardiograms from Case 8 (girl aged twenty years; thyrotoxicosis). February 19, 1929, before thyroidectomy; showing inversion of T in Leads II and III. March 1, 1930, after thyroidectomy; showing upright T in Lead II and isoelectric T in Lead III.

THYROTOXICOSIS

This group comprises 4 patients, 1 male and 3 females, with an average age of twenty-four and one-half years. Each presented signs and symptoms characteristic of uncomplicated thyrotoxicosis. The heart was very slightly enlarged in two, and in one the systolic blood pressure was abnormally high—164 mm. mercury systolic and 50 mm. diastolic. Following subtotal thyroidectomy the heart size and blood pressure in these instances returned to normal. No other diagnosis was made in the case of any of these patients while under our care.

The initial electrocardiograms were taken shortly after entry into the hospital and before the administration of iodine, at which time

the average basal metabolic rate was plus 44. In three instances T was upright in Lead I, and inverted in Leads II and III. In one instance T was isoelectric in Lead I, and inverted in Leads II and III. The average heart rate, measured from the electrocardiograms, was 140. There were no other significant electrocardiographic abnormalities.

Following subtotal thyroidectomy each patient experienced relief from the distressing symptoms, and the basal metabolic rates returned to normal. Reexamination later revealed nothing abnormal, and the electrocardiograms showed upright T in Leads I and II in each instance.

Comment.—It is not generally agreed that T varies in form or direction in thyrotoxicosis. Hoffman[2] and others since have described the association of a high T-wave with this condition; whereas Lewis[3] could find no definite alteration in the shape of the ventricular complex. White and Aub[4] found only very limited parallelism between the basal metabolism and the amplitude of T in 27 patients with thyrotoxicosis. Willius[5] and his coworkers reported inversion of T in 5 instances of thyrotoxicosis but believed coronary disease responsible. More recently, Pardee[6] has written that "curves resembling the coronary T-wave may be seen [in hyperthyroidism]. When the toxicity passes off, the T-wave of these patients will return to normal."

In the cases we present, the evidence is presumptive that the thyrotoxicosis was responsible for the inverted T. Whether or not there was in these patients some degree of relative coronary insufficiency, not however causing angina pectoris but dependent on the thyrotoxicosis, we have no way of knowing. It is true that infrequently relatively young patients with thyrotoxicosis suffer from angina pectoris which disappears when the basal metabolic rate returns to normal.

INFECTION

This group comprises 5 patients, 1 male and 4 females, with an average age of twenty-five years. Each suffered from some infection (not rheumatic or diphtheritic) either shortly before or at the time of the initial examination. None had any cardiac complaint, and at no time was there clinical evidence of organic heart disease. No abnormality in size or shape of the heart was found. In two, slight inconsequential systolic murmurs were heard. The blood pressures of all were normal. In 3 of the 5 patients the initial electrocardiogram showing an inverted T was taken during the illness, while in the remaining two it was taken six weeks and four months, respectively, after the infection. T in Lead I was upright in all instances, T in Lead II was inverted in three and diphasic in two, and T in Lead III was inverted or diphasic in all. The average heart rate, measured from the electrocardiograms, was 115. There were no other significant electrocardiographic abnormalities. One patient died on the day the electrocardio-

gram was taken; the heart was judged normal at necropsy. Three of the remaining four became well; and electrocardiograms, taken two, two and one-half, and twelve months, respectively, after the infection, showed normal T-waves in Leads I and II and inverted T-waves in Lead III. The remaining patient (Case 12) at the time of reexamination had a mild recrudescence of her chronic bronchopulmonary infection, and the electrocardiogram showed sinus arrhythmia, rate 110, upright T in Lead I, slightly upright T in Lead II and inverted T in Lead III. Some details concerning the return from an inverted to an upright T can be gained from the case summaries.

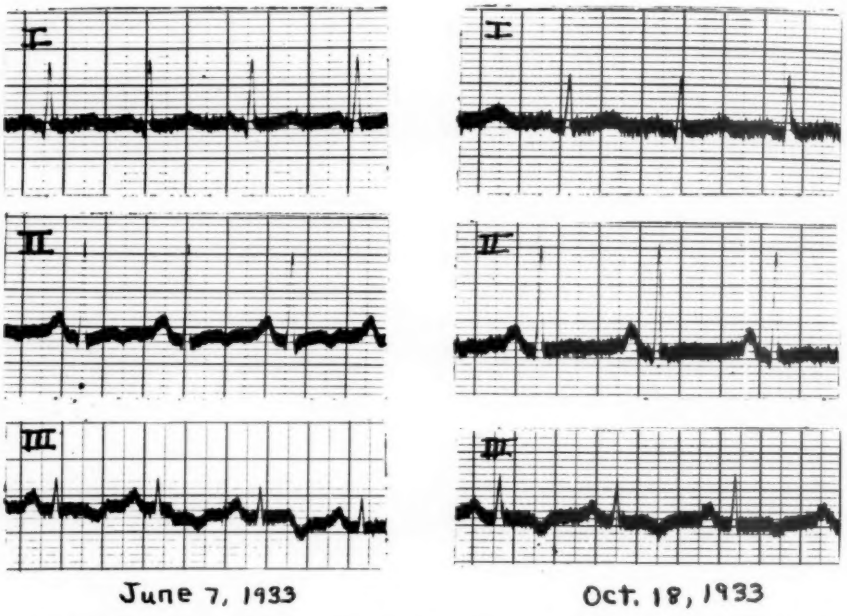

Fig. 3.—Electrocardiograms from Case 12 (woman aged twenty-seven years; chronic bronchopulmonary suppuration). June 7, 1933, during acute phase; showing inversion of T in Leads II and III. October 18, 1933, during mild recrudescence; showing slightly upright T in Lead II and inverted T in Lead III.

Comment.—Since the time of Kraus and Nicolai[7] (1910) it has been known that the T-wave may be depressed by the action of heart poisons. The first observations illustrating the effect of infections in depressing the T-wave of the electrocardiogram of human beings were made by Smith,[8] who published records showing inversion of T in Leads I and II following diphtheria. Later Cohn and Swift[9] showed that inversion of T may occur in acute rheumatic fever. More recently inversion of T has been shown to occur in relation to various infections. This relationship of the heart to infections is sometimes declared by certain clinical signs or symptoms, but at other times the chief or sole discoverable sign is furnished by the electrocardiogram.

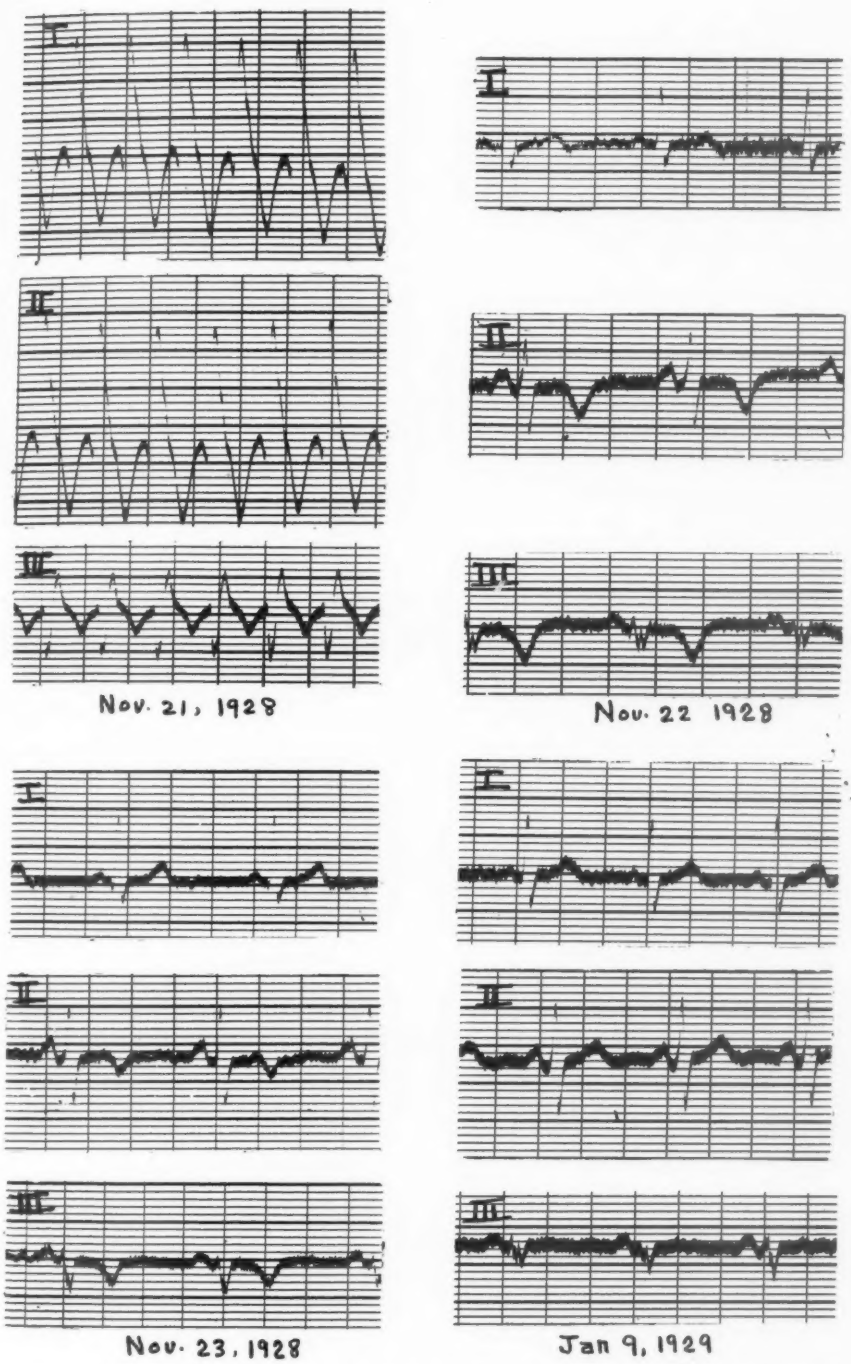

Fig. 4.—Electrocardiograms from Case 17 (man aged thirty-three years; paroxysmal ventricular tachycardia). November 21, 1928, showing the abnormal rhythm. November 22 and 23, 1928; normal rhythm with inversion of T in Leads II and III. January 9, 1929; T in Lead II is now upright and in Lead III isoelectric.

PAROXYSMAL VENTRICULAR TACHYCARDIA

This group comprises two young men in robust health. In both, the only evidence of cardiac disability was furnished by a single paroxysm of ventricular tachycardia lasting less than twenty-four hours. The onset of the paroxysm was not provoked by any unusual incident in either case; the offset occurred spontaneously in one and after 9 grains of quinidine sulphate in the other. In one the first electrocardiogram taken after the paroxysm showed normal rhythm at a rate of 52, inversion of T in Lead I, high T in Leads II and III, short P-R interval with widened QRS complexes,[1] and right axis deviation. In the other, the first electrocardiogram taken after the paroxysm showed normal rhythm at a rate of 80, upright T in Lead I and inverted T in Leads II and III. Both individuals were examined repeatedly over a period of two months and two years, respectively, and no physical abnormality was detected. Later electrocardiograms taken at intervals showed a gradual return of the abnormally inverted T-waves to the upright form.

Comment.—We believe the paroxysms of ventricular tachycardia to be in some way responsible for the temporary inversion of the T-waves. However, on looking over the tracings of all our other cases showing paroxysmal ventricular tachycardia or paroxysmal auricular tachycardia, flutter, or fibrillation, we were unable to find further examples.

MISCELLANEOUS

This group comprises five patients with an average age of twenty-six years. One had no disease of any nature; the diagnosis in the remainder was either complicated or not made. The case summaries may be referred to for details. The initial electrocardiograms all showed inversion of T in Leads II and III and an average heart rate of 119. At the time of our last examination the electrocardiogram in each case showed upright T in Leads I and II, and an average heart rate of 102.

Comment.—Each patient in this group presented a problem in diagnosis. With two exceptions, in whom infection (in one of them diphtheria one year before) may have played a rôle, an explanation for the inverted T-waves is not to be found in medical writings. It is thus evident that on rare occasions one finds inversion of T in Leads I and II without apparent cause.

FURTHER DISCUSSION

The T-wave is much less stable than the other electrocardiographic deflections. Although its mechanism is obscure, we are familiar with certain secondary factors that may change its form and direction.

Chief among these are alterations of coronary circulation, disturbances of nervous origin, the action of toxins or drugs, and change in position of the heart.

We are not unmindful that one sometimes finds extensive coronary sclerosis at post-mortem examination in young individuals who may or may not have had symptoms of coronary origin. However, in the cases herewith presented we were unable to determine that the coronary circulation was inadequate either as the result of the particular condition diagnosed or independent of it. We are not even justified in assuming a relative coronary insufficiency with the heart working under unfavorable conditions.

Human and animal observations agree in showing that T may alter through nerve stimulation or depression. The accelerated heart rate recorded in many cases in this series was not always adequately explained, and it is interesting that sometimes the change from inverted to upright T was associated with a fall in rate.

With the possible exception of those cases in which infection was present there was no evidence of toxic injury to the myocardium. Likewise there was no evidence of drug intoxication, or that change in position of the heart had occurred.

Thus we have found that inversion of T in Leads I or II is by no means invariably allied with causes commonly held to produce such inversion. We have selected instances in which neurocirculatory asthenia, thyrotoxicosis, infection, or paroxysmal ventricular tachycardia was the only associated finding. This association is presented without concluding that the above disorders are even secondarily responsible for T inversion. Of chief importance is the correct interpretation of the electrocardiographic findings which must still be done by correlation with the patient's history and physical examination. To emphasize the correctness of our interpretation we have included only patients in a young age group and those whom we have observed over a considerable period of time. It is not unreasonable to assume that some such patients are now wrongly thought to have serious organic heart disease. Many others in whom there was strong presumptive evidence that significant heart disease did not exist were not included in this series because of their greater age or their failure to return for reexamination.

The T-wave in Lead III was more inverted than the T-wave in Lead II in each instance recorded above, and remained inverted in most instances (16 out of 23) after the T-wave in Lead II had ceased to be inverted. It is well recognized by those dealing with routine electrocardiography that the inversion of T in Lead III is frequently found in normal individuals.

SUMMARY

1. We have presented 23 cases in which significant inversion of the T-wave of the electrocardiogram was not associated with the usual known causes for such inversion.

2. The reason for T inversion in these cases is unknown.

3. The importance of this finding is that it points to the need of caution in the diagnosis of serious heart disease when inversion of the T-wave in Lead II of the electrocardiogram is the only abnormal finding.

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ARTERIOLAR LESIONS OF SKELETAL MUSCLE IN HYPERTENSION*

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IT IS now well established that individuals dead of so-called essential hypertension usually show a more or less severe involvement of the smaller renal arteries—the arterioles. Similar lesions of the arterioles are often found in other organs, i.e., liver, spleen, pancreas, adrenals, intestines, nervous system, and retina, but opinions differ as to the occurrence of such lesions in somatic muscle. Most observers in the past, notably Jores, Fahr and, in this country, Bell and Fishberg, have reported that the voluntary muscles in hypertensive disease rarely show arteriolar lesions. Recently, however, Keith and his associates, using as their criterion the quantitative relationship between the thickness of the vessel wall and the diameter of the lumen, reported arteriolar lesions in voluntary muscle in certain types of hypertension.

In this work we have rated arterioles not according to deviation from Keith's normal ratio but according to the examiner's concept of what constituted a diseased vessel. All ratings were made by one of us (D.P.S.), and our criteria, so far as they can be expressed in units, are (1) thickening of the vessel wall, (2) hyalinization of vessel wall, (3) other pathological changes such as fatty, fibrous and necrotizing lesions, (4) size of lumen. A standard hematoxylin and eosin stain following formalin fixation was used throughout. In this work care was taken to rate only the smallest vessels. A case was rated according to the severest lesion observed, regardless of variation in the same section or in sections from different voluntary muscles in the same section. Our ratings were from one to four plus. We believe that a vessel rating three to four plus by our criteria would be regarded by most pathologists as a seriously diseased arteriole.

Sections of skeletal muscle were taken from 426 cases and the arterioles were rated objectively, with no knowledge on the part of the observer of the clinical diagnosis in the case. The patients varied in age from the first day of life to the ninth decade. Time will not permit a detailed discussion of this material, but one interesting fact appears established, namely that in 68 per cent of a series of 386

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autopsies there was a definite relation between the state of the arterioles in the kidney and those in the skeletal muscle.

Included in the above material was a series of cases of diffuse vascular disease with hypertension, carefully studied clinically. We include for discussion here only those patients dying under the age of forty-six years. This arbitrary age limit was set in order to eliminate the possible rôle of an age factor in arteriolar disease. The pertinent data in this series are shown in Tables I and II.

TABLE I

ARTERIOLES IN SKELETAL MUSCLES AND KIDNEY IN 24 AUTOPSIED CASES OF HYPERTENSION, PATIENTS UNDER FORTY-SIX YEARS OF AGE

NAME	AGE	SEX	RACE	MEAN BLOOD PRESSURE		ARTERIOLES		CAUSE OF DEATH	HEART WEIGHT GRAMS
				SYSTOLIC	DIASTOLIC	MUSCLE	KIDNEY		
C. G.	30	F	Black	220	140	3-4+	4+	Uremia	425
E. W.	33	F	Black	240	150	3-4+	3-4+*	Uremia	400
F. J.	33	F	Black	170	120	2-3+	2-3+	Cardiac	400
M. T.	35	F	Black	240	110	1+	3-4+*	Uremia	575
L. B.	35	F	Black	260	160	3-4+	4+*	Uremia	475
M. M.	38	F	Black	215	140	2+	3-4+*	Uremia	375
M. C.	39	F	Black	225	125	4+	3-4+	Cerebral hemorrhage	425
E. M.	40	F	Black	250	180	3-4+	3-4+	Pneumonia	375
M. G.	40	F	Black	230	125	2+	2-3+	Cardiac	700
M. D.	41	F	Black	210	125	3+	4+*	Uremia	625
R. R.	27	M	Black	190	130	4+	3-4+*	Uremia	650
L. W.	37	M	Black	210	150	3-4+	4+*	Uremia	†
C. H.	37	M	Black	240	160	1+	3-4+*	Cardiac	675
J. S.	39	M	Black	220	140	2-3+	4+*	Cardiac	650
J. L.	42	M	Black			2-3+	2-3+*	Uremia	650
W. J.	43	M	Black	210	145	2+	4+*	Pneumonia	500
O. D.	45	M	Black	240	150	3-4+	4+*	Uremia	570
H. T.	32	F	White	230	150	2-3+	3-4+	Cardiac	650
D. B.	33	F	White	230	130	3-4+	3-4+	Cardiac	600
C. N.	41	F	White	230	145	3-4+	3-4+*	Uremia	425
J. C.	44	F	White	220	120	3+	3+	Cerebral hemorrhage	400
P. H.	45	F	White	220	120	4+	4+	Uremia	450
E. K.	35	M	White	195	155	2-3+	4+	Cardiac	500
E. B.	37	M	White	220	130	2+	3+	Cerebral hemorrhage	500

*Necrotizing arteriolar lesions.
†Heart not obtained.

In Table I are the data on 24 necropsied cases in which the arteriolar lesion of skeletal muscle is compared with that of kidney. In Table II are data on 25 cases in which were were unable to secure a necropsy but in which a biopsy specimen of the pectoralis major muscle was studied. Of those individuals dying under observation in this series the cause of death is indicated.

Clinical aspects of the two groups may be considered as follows. *Age:* As mentioned above, all patients were under forty-six years of age. The youngest was sixteen years. The average age at death was 36.2 years. *Race:* Noteworthy is the preponderance of negroes. In

spite of the fact that our hospital population is less than 25 per cent colored, fatal hypertensive disease under forty-six years of age occurred about three times as often in the black as in the white race. *Sex:* There were 30 females and 19 males. The widely held view that vascular disease is more prevalent in males than in females is not confirmed by this series. Thirty, or 61 per cent, of the patients were females and 19, or 39 per cent, were males. Twenty females were black and 10 white; 17 males were black and only 2 were white. In both

TABLE II

ARTERIOLES IN SKELETAL MUSCLE (BIOPSY) IN 25 FATAL CASES OF HYPERTENSION, PATIENTS UNDER FORTY-SIX YEARS

NAME	AGE	SEX	RACE	MEAN BLOOD PRESSURE		ARTERIOLES BIOPSY MUSCLE	CAUSE OF DEATH
				SYSTOLIC	DIASTOLIC		
A. C.	26	F	Black	175	130	2-3+	Uremia
G. C.	28	F	Black	200	135	3+	
E. W.	28	F	Black	235	155	2-3+	Cardiac
I. N.	29	F	Black	180	124	3-4+	
N. D.	37	F	Black	220	145	3-4+	
A. S.	38	F	Black	185	130	3-4+	
M. P.	39	F	Black	235	165	2-3+	Uremia
M. T.	39	F	Black	190	140	3+	
E. B.	40	F	Black	195	135	3+	
C. D.	43	F	Black	235	165	3-4+	Cardiac
F. S.	23	M	Black	195	145	2-3+	Cardiac
L. S.	30	M	Black	180	118	2+	
B. F.	32	M	Black	170	135	3+	Cardiac
E. S.	32	M	Black	220	170	2-3+	Uremia
E. M.	36	M	Black	190	120	1-2+	
W. W.	33	M	Black	260	135	2-3+	Uremia
S. W.	39	M	Black	180	120	3-4+	
C. S.	41	M	Black	195	118	4+	
J. O.	42	M	Black	235	180	2-3+	Cardiac
F. B.	45	M	Black	170	100	3+	
J. W.	16	F	White	212	155	2-3+	Uremia
M. R.	32	F	White	220	145	2-3+	Cardiac
T. C.	30	F	White	230	140	3-4+	
R. M.	43	F	White	215	135	4+	
M. C.	40	F	White	240	165	2+	Uremia

races, therefore, in this series the females predominate. *Blood pressure:* The blood pressure readings represent the average of a number of determinations of the systolic and diastolic blood pressures during the period of clinical observation. In most instances the systolic pressure was above 200 mm. and the diastolic above 120 mm. of mercury, illustrating the well-known fact that the hypertension associated with diffuse vascular disease is as a rule higher than that in glomerular nephritis.

Reference to the necropsied group (Table I) shows a significant parallelism between the arteriolar lesion in the kidney and that in the skeletal muscle. In six instances the muscle lesion was slight, rated one to two plus, whereas the kidney lesion in these instances was

severe. In 13 of the 24 cases, necrotizing arteriolar lesions were found in the kidneys. Twelve, or 50 per cent, of the patients died in uremia. This high incidence of uremia is greater than that found in hypertensive patients of all ages, and is due in our opinion (1) to the large percentage of negroes in the group and (2) to the fact that we deal only with patients dying under forty-six years of age. In other words, the high incidence of death from renal insufficiency here suggests that the arteriolar lesion in the kidney in the earlier decades of life and particularly in the negro race is more severe or pursues a more fulminating course than in the other vascular regions.

In the nonautopsied group (Table II) our observations on the arterioles of skeletal muscle were limited to the biopsy specimen. The frequency and severity of arteriolar lesions is apparent, for in only 3 cases were the lesions rated two plus or less by our criteria.

TABLE III

ARTERIOLES IN SKELETAL MUSCLE (BIOPSY AND AUTOPSY) AND IN KIDNEY IN 10 CASES OF HYPERTENSION, PATIENTS UNDER FORTY-FOUR YEARS

NAME	AGE	SEX	RACE	MUSCLE		KIDNEY	DEATH DUE TO
				BIOPSY	AUTOPSY		
C. G.	30	F	Black	3-4+	3-4+	4+	Uremia
E. W.	33	F	Black	3+	3-4+	3-4+*	Uremia
L. B.	35	F	Black	4+	3-4+	4+*	Uremia
M. G.	40	F	Black	3-4+	2+	2-3+	Cardiac
M. D.	41	F	Black	3-4+	3+	4+*	Uremia
M. D.	43	F	Black	4+	4+	†	Uremia
R. R.	27	M	Black	4+	4+	3-4+*	Uremia
J. S.	39	M	Black	3-4+	2-3+	4+*	Cardiac
W. J.	43	M	Black	2-3+	2+	4+*	Pneumonia
D. B.	33	F	White	3+	3-4+	3+	Cardiac

*Necrotizing arteriolar lesions.
†Autopsy restricted to thorax.

In Table III are data on 10 cases in which both a biopsy and an autopsy section of skeletal muscle were compared. This was done in order to check the reliability of our technical methods and also to study the question of whether or not the technic employed in removing a section of living muscle could introduce artefacts which might be interpreted as a lesion of the vessel wall. Our data show conclusively that the appearance of the arteriole in skeletal muscle in a biopsy specimen is practically identical with that seen in the autopsy specimen of the same case. It is apparent also that in this group the severity of the vascular lesion in the kidney agreed closely with that observed in both the biopsy and the autopsy specimen of skeletal muscle.

CONCLUSIONS

Observations on the foregoing group of cases appear to warrant these conclusions:

1. Arteriolar lesions in skeletal muscle are demonstrable in a high percentage of individuals dying under forty-six years of age of diffuse vascular disease with hypertension.

2. The severity of the muscular lesion in such cases usually parallels the severity of the arteriolar lesion of the kidney.

3. The arteriolar lesion in a biopsy specimen of voluntary muscle agrees closely in severity with that found in a post mortem specimen of the same muscle.

4. Our studies of blood vessels confirm the opinion reached some years ago from our clinical observations, that the vascular system of the negro is more vulnerable than the white man's to the noxious agent or agents responsible for the diffuse vascular lesions so often associated with chronic hypertension.

CIRCULATORY STUDIES ON A CASE OF ARTERIOVENOUS ANEURYSM

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THE deleterious influence of arteriovenous fistulas upon the heart was first demonstrated by Reid[1] in a series of interesting survival experiments on animals. Following the production of large arteriovenous communications in dogs, cardiac hypertrophy and dilatation and the evidence of myocardial insufficiency developed. This investigation was prompted by Reid's clinical experience with patients with arteriovenous aneurysms. In two such cases cardiac hypertrophy and dilatation had been noted by Osler and Halsted, but no causal relationship was considered.

The present knowledge of the pathological physiology associated with such fistulas is in large measure due to Reid,[2] Holman,[3] Lewis and Drury,[4] but certain of the phenomena associated with this interesting condition are still incompletely understood.

The results of the study of this case added a new observation to the published data regarding arteriovenous aneurysms. In general, our findings are in accord with the excellent clinical and experimental work of Holman, but differ in several respects from the investigations of Lewis and Drury.

CASE REPORT

The patient, a white male of twenty-three years, was shot in the right leg two years before. One bullet penetrated the anterior surface of the right lower leg over the tibia, and another entered the medial posterior portion of the right thigh and emerged laterally and posteriorly to the femur four inches above the knee. There was severe hemorrhage above the right knee at the time of the accident, enormous swelling of the thigh and shortly afterward the appearance of an ulcer on the anterior surface of the tibia where one of the bullets entered the leg. Since then the patient had been incapacitated because of pain and swelling of the injured leg. There had been some precordial pain, palpitation, effort dyspnea, and profuse sweating of the right leg.

When the patient was first seen the blood pressure was 130/60 mm. Hg, pulse 84, and temperature normal. There was moderate enlargement of the heart, confirmed by teleroentgenogram, and a soft systolic murmur at the cardiac apex.

The right leg was markedly edematous. There were numerous engorged, tortuous veins over the anterior surface of the right tibia and around the knee, and three ulcers in the skin of the lower portion of the right leg (Fig. 1). The right popliteal space was unusually full and pulsated with each heartbeat. The right femoral artery as it emerged beneath Poupart's ligament was markedly enlarged

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in comparison to the left femoral artery which was apparently normal in size. The right leg was swollen and wet with perspiration from the knee to the foot, while the left leg was dry. A marked systolic thrill was felt over the popliteal space, and a continuous roaring murmur with marked systolic intensification was heard over this area. Pressure sufficiently strong to obliterate the femoral artery caused an immediate drop in the pulse from 85 to 50* and the blood pressure rose on several occasions from 110/60 to 130/70 with disappearance of the thrill and murmur. It was clear from these facts that the patient had a fistulous communication between the popliteal artery and vein.

Fig. 1.—Popliteal arteriovenous aneurysm; duration two years.

As Lewis has stated that the sudden fall in the rate of the pulse when an arteriovenous aneurysm is occluded is of vagal origin,[4] we administered atropine sulphate, gr. $\frac{1}{33}$, to paralyze vagus activity. In thirty minutes the maximum acceleration of the pulse occurred (rate 130), and the fistula was occluded by digital pressure. The pulse rate immediately fell to 114. An hour later with the rate 107, occlusion

*In a most interesting paper published in the Emanuel Libman Anniversary Volume, 1932. Dean Lewis discusses the history of "The Bradycardiac Reaction and the Cardiac Changes in Arteriovenous Aneurysms," and states that the bradycardiac reaction was first described by Nicolodoni in a congenital arteriovenous aneurysm, which he reported under the title of "Phlebarteriectasie der rechten oberen Extremität," in the Arch. f. klin. Chir. 18: 252, 1875. Fifteen years later Brasham described the same reaction in a traumatic arteriovenous aneurysm involving the femoral artery.

caused a decrease in pulse rate to 94. The blood pressure which was 122/80 mm. when the pulse rate was 107, rose 10 mm. in the diastolic reading following occlusion, while the systolic pressure was not influenced. This rise in diastolic pressure and stability of the systolic level persisted during the period of atropine influence.

That the blood pressure falls and the pulse rate increases immediately upon the opening of a large arteriovenous fistula, has been frequently demonstrated. Bainbridge[6] has shown that increased venous return to the heart and, consequently, an increase in the pressure in the great veins and right auricle cause an acceleration of pulse rate, while Marey's law states that, other conditions remaining the same when arterial pressure is raised, the heart is slowed and vice versa, i.e., the pulse rate varies inversely as the arterial pressure.

The Bainbridge reflex is probably responsible for the acceleration of rate immediately after an arteriovenous fistula is opened. In all likelihood the reflex cardiac acceleration is caused by afferent impulses traveling up the vagi from the auricles and reducing the tone of the cardio-inhibitory center. The reduction of vagus tone, however, may occur from carotid sinus and aortic reflexes. The third possibility is the direct stimulation of the cardio-accelerator mechanism.

Lewis and Drury[4] in summarizing their studies of five patients with arteriovenous aneurysm state that "the leak from artery to vein has no appreciable effect on general venous pressure," and "in those cases in which the arteriovenous anastamosis could be cut off at will this procedure failed to alter the venous pressure in measurable degree."

Our results were not in accord with these conclusions, and the readings of venous pressure obtained independently by different observers and by different methods were practically identical.

TABLE I

VENOUS PRESSURE DETERMINATIONS
(INDIRECT MEASUREMENTS)

	BEFORE OCCLUSION OF FISTULA	AFTER OCCLUSION
Left arm	57 mm. H_2O	62 mm. H_2O
Right arm	62 mm. H_2O	68 mm. H_2O
Right leg (above fistula)	62 mm. H_2O	
Right leg (below fistula)	60 mm. H_2O	85 mm. H_2O

VENOUS PRESSURE
(DIRECT METHOD)

	BEFORE OCCLUSION OF FISTULA	AFTER OCCLUSION
Left arm	60 mm. H_2O	95 mm. H_2O

The average increase in the venous pressure that followed digital occlusion of the fistula was 30 mm. of water.

From the theoretical standpoint it seems probable that the sudden diversion of a large amount of blood from the heart-artery-vena-cava circulation to the heart-artery-capillary-vein circulation would suddenly increase the volume of venous blood in the periphery and necessarily increase pressure. Harrison[5] has proved that there is a very marked increase in cardiac output in animals with arteriovenous communications, and Holman has shown that the blood volume is greatly aug-

Fig. 2.

mented in the presence of large fistulous communications between arteries and veins. Thus the gradual dilatation and hypertrophy of the heart which occurs in the presence of large arteriovenous fistulas in human beings and in animals with large fistulas is explicable.

Fig. 2 shows the appearance of proximal and distal vessels and the arterial aneurysm opposite the fistula and Fig. 3 the successful extirpation of the arteriovenous fistula by Dr. Mont R. Reid. Following the operation the blood supply to the affected leg and foot improved im-

mediately, and in a few hours the pulsations in the dorsal pedis and posterior tibial arteries were readily palpable. Within a few days healing of the chronic leg ulcers began. There was a prompt and marked decrease in edema. The size of the heart showed a remarkable decrease (Figs. 4 and 5). This reduction in the cardiac diameter was probably dependent upon a decrease in the work requirements and in total blood volume. An immediate and permanent rise in diastolic pressure and a subsequent fall in the systolic pressure followed the opera-

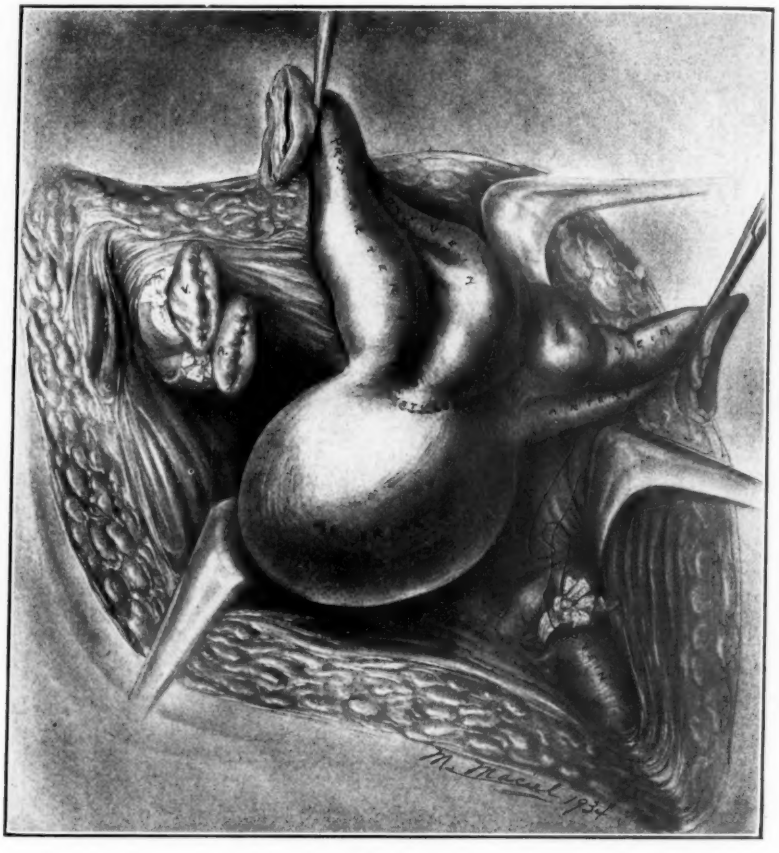

Fig. 3.

tion and were obviously consequent upon the replacement of normal peripheral resistance. The pulse rate returned to normal probably because of the abolition of an excessive return of venous blood to the heart. Associated with these circulatory readjustments the symptoms of myocardial insufficiency disappeared completely. The dilatation of the artery proximal to the fistula, in our opinion, has not been completely explained by Holman's hypothesis of compensatory dilatation because of increased blood volume flow; as the walls of the artery in our case were

thinner than normal, and there was a decided atrophy of the muscular elements of the arterial wall. Atrophy in a healthy structure in the presence of the necessity for increased work seems a biological paradox. Perhaps, as Reid believes, the lowered diastolic pressure in the proximal portion of the vessel decreases the blood supply to the walls of the artery, or the combination of the necessity of the vessel to carry a larger amount of blood without the requirement of the diastolic pressure usually maintained in large arteries may explain the mutation of the artery to a veinlike structure.

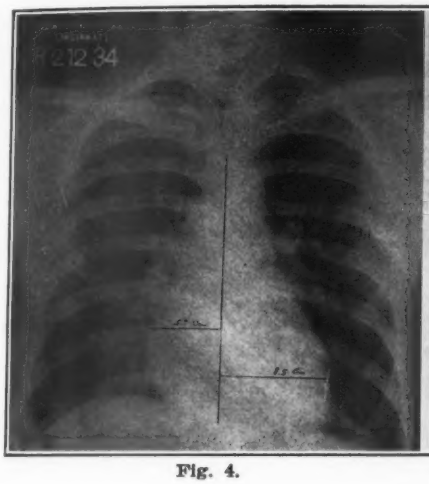

Fig. 4.

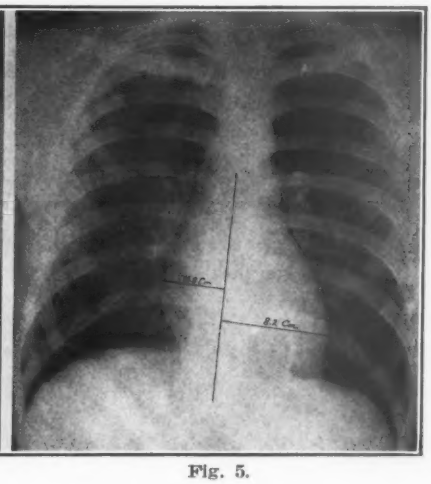

Fig. 5.

CONCLUSIONS

1. The establishment of a large arteriovenous communication between the popliteal artery and vein in a healthy young man was accompanied by: (a) an increase in systolic and a decrease in diastolic blood pressure levels; (b) cardiac and aortic dilatation and the symptoms of myocardial insufficiency; (c) dilatation and atrophy of the artery proximal to the arteriovenous communication, and hypertrophy of the vein in the area contiguous to the fistula, an arterial aneurysm opposite the fistula; (d) evidence of peripheral vascular malnutrition below the fistula, i.e., edema, ulceration of the skin, superficial varicosities, decrease in surface temperature, and decreased pulsation of the dorsalis pedis and posterior tibial arteries.

2. Digital occlusion of the fistulous communication produced: (a) bradycardia, and an immediate elevation of the diastolic and systolic arterial pressure; (b) definite elevation of the systemic venous pressure, i.e., antecubital vein; (c) slight decrease in the size of the heart as seen fluoroscopically.

3. Operative extirpation of the arteriovenous fistula caused: (a) the disappearance of symptoms of myocardial insufficiency; (b) a marked decrease in the size of the heart; (c) after the initial rise, a gradual drop in the systolic, and a permanent rise in the diastolic arterial blood pressure to normal levels; (d) diminution of peripheral edema in the affected leg, healing of the leg ulcers, the appearance of adequate arterial circulation in the foot.

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A CLINICAL AND PATHOLOGICAL STUDY OF CORONARY SCLEROSIS: ITS INCIDENCE IN HYPERTENSION AND ANGINA PECTORIS*

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WITH the focusing of attention upon disease of the coronary arteries in recent years, it has become evident, as the result of both clinical and autopsy studies, that the condition with which it is most often associated is arterial hypertension. At the autopsy table, coronary arteriosclerosis has been found in 90 per cent of hypertensive patients (Bell and Clawson[1]) whereas in routine autopsies on individuals of all ages it occurs in from 25.9 per cent (Tery[2]) to 37.1 per cent (Allan[3]), and in from 39.6 per cent (Bell and Clawson[1]) to 50 per cent (Rössle[4]) of persons over the age of forty-five years. There are in the literature few verified statements as to whether it may occur as an isolated phenomenon or more often concurrently with disease in other areas of the arterial bed. Bell and Clawson[1] found that in their series of hypertensive patients the frequency of renal arteriosclerosis in the coronary group was less than that in the "myocardial" and "encephalic" groups. Bork,[5] on the other hand, believes that from the middle of the fourth decade of life a parallelism exists between arteriosclerosis of the coronary and peripheral arteries.

Clinically, such relationships are difficult to unravel because so often the symptomatology of coronary disease in essential hypertension is confused by the presence of a fatigued but adequately irrigated myocardium. The string galvanometer has proved of value in detecting myocardial damage consequent upon coronary narrowing or occlusion in arteriosclerotic heart disease, but the exact significance, as regards the condition of the coronary arteries, of many electrocardiographic abnormalities encountered in arterial hypertension demands further study.

We have investigated three groups of patients in an attempt to throw light upon the following questions.

1. What is the incidence of clinically detectable coronary sclerosis in essential hypertension?

2. What is the relationship, if any, between the occurrence of coronary disease and changes of the peripheral vessels, aorta and arterioles in this condition?

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3. What is the nature and significance of the electrocardiographic changes encountered in essential hypertension?

METHOD

The following groups of patients have been studied.

I. *Ninety persons with essential hypertension.* The incidence and distribution of clinically ascertainable vascular disease, in addition to the symptoms and signs (including routine electrocardiograms) of coronary sclerosis were determined. The peripheral vessels were palpated in all instances. The ocular fundi were examined. The status of renal function, as a measure of arteriolar disease of the kidneys, was determined by the following tests: (1) P.S.P.; (2) water test of Volhard; (3) urea clearance; (4) level of urea in the blood; and (5) in many instances, the creatinine excretion test of Major and the renal test meal of Hedinger-Schlayer. Renal function was not considered to be impaired unless at least two of these tests gave abnormal results.

II. *Sixty-five hypertensive patients dying either of vascular disease or of unrelated causes.* The post-mortem incidence of coronary sclerosis was determined. Only an actual arteriosclerotic narrowing of the coronary vessels, with or without myomalacia or fibrous change of the myocardium, was regarded as significant. The clinical criteria, to be described later, for the presence of coronary sclerosis as applied to the first group were in this series checked against the post-mortem findings. The incidence of coronary change was correlated with that of arteriosclerosis of the aorta and arteriolar sclerosis of the renal vessels as determined by the microscope.

III. *One hundred and ten patients with angina pectoris, 10 of whom came to autopsy.* The incidence of peripheral and aortic sclerosis, together with the electrocardiographic findings, was contrasted with that in the preceding groups and with the findings in a series of 23 autopsied instances of coronary occlusion.

RESULTS

The essential data are given in Table I. Clinically, we have regarded the presence of angina pectoris, cardiac asthma, coronary occlusion, or, in their absence, electrocardiographic changes (to be discussed later) as presumptive evidence of coronary sclerosis. In the first group of 90 persons having essential hypertension such changes were encountered in 34 (37.7 per cent), distributed as follows: angina pectoris, 7 instances; cardiac asthma, 6 instances; coronary occlusion, one instance; electrocardiographic abnormalities only, 20 instances. The average age of these patients was slightly greater than that in the remainder of this series, and males were predominantly affected.

TABLE I

DISTRIBUTION OF VASCULAR CHANGES IN ESSENTIAL HYPERTENSION, ANGINA PECTORIS, AND CORONARY OCCLUSION

	HYPERTENSION (155 CASES)				ANGINA PECTORIS (110 CASES)		CORONARY OCCLUSION (23 CASES)
	CLINICAL		POSTMORTEM				
	WITH CLINICAL COR. SCL.	WITHOUT CLINICAL COR. SCL.	WITH CLINICAL COR. SCL.	WITHOUT CLINICAL COR. SCL.	CLINICAL	POSTMORTEM	POSTMORTEM
Number of cases	34	56	35	30	100	10	23
Age, years	45-90	22-79	39-85	27-87	31-88	55-85	40-76
	Av. 63.4	57.8	63.0	61.9	60.5	66.8	63.0
Sex Male	19	18	24	17	55	7	16
Sex Female	15	38	11	13	45	3	7
					41% with hypertension / 59% without hypertension	Hypertension in 70%	Hypertension in 39.1%
Percentage of peripheral arteriosclerosis	100.0 ± 1.4	71.8 ± 4.2	—	—	90.6 ± 5.3 / 48 ± 7.0	90 ± 9.4	100.0 ± 2.0
Percentage of aortic arteriosclerosis	52.9 ± 8.5	24.5 ± 3.2	100 ± 1.7	86.6 ± 6.0	14.8 ± 3.8	90 ± 9.4	100.0 ± 2.0
Percentage of coronary arteriosclerosis (postmortem)	—	—	97 ± 2.8	66.6 ± 8.5	—	90 ± 9.4	100.0 ± 2.0
Percentage of arteriolosclerosis (fundi; kidneys)	94.1 ± 4.0	66.1 ± 6.3	100 ± 1.7	96.6 ± 3.0	?	90 ± 9.4	69.5 ± 9.6

The average duration of elevated blood pressure (8.8 ± 1.0 year), according to the history in 20 instances, was significantly greater than the figure of 4.5 ± 0.7 year in 21 instances without evidence of coronary sclerosis. There is a statistically significant difference in the incidence of changes in the peripheral vessels, in the aorta (as determined by fluoroscopy), and in renal function in those patients with and without clinical evidence of coronary sclerosis. Widespread vascular damage is more evident in the group having coronary sclerosis. The series of patients with essential hypertension coming to necropsy was divided into two groups, depending on the clinical evidence of presence or absence of coronary sclerosis. The presumptive clinical evidence of coronary disease was distributed as follows: angina pectoris in 12 patients; cardiac asthma in 13; coronary occlusion in 7; electrocardiographic abnormalities only (from a total of 27 tracings) in 3 patients. Thus 35 patients, in a total group of 65, had clinical evidence of coronary disease. In 97 per cent ± 2.8 per cent the clinical impression was substantiated by the post-mortem findings. There was one exception only, a patient with cardiac asthma whose coronary arteries were only slightly diseased. However, well-marked coronary sclerosis was present in over half (66.6 ± 8.5 per cent) of the patients who came to post-mortem examination in whom our clinical criteria for its presence were not met. Aortic sclerosis was significantly more common in the coronary group; whereas renal arteriolosclerosis, with the exception of one instance in which the kidney was not examined microscopically, was a universal finding.

TABLE II

PERCENTAGE OF DISTRIBUTION OF PERIPHERAL ARTERIOSCLEROSIS AND ARTERIOLOSCLEROSIS

		HYPERTENSION—90 PATIENTS	
		WITH CLINICAL CORONARY SCLEROSIS 34 CASES	WITHOUT CLINICAL CORONARY SCLEROSIS 56 CASES
Peripheral arteriosclerosis	None	0.0 ± 1.7	28.3 ± 6.0
	Temporal	50.0 ± 8.5	39.6 ± 6.5
	Brachial	41.1 ± 8.4	20.7 ± 5.3
	Radial	79.4 ± 6.9	58.4 ± 6.5
	Dorsalis pedis	20.5 ± 6.8	22.6 ± 5.5
Arteriolosclerosis	None	5.8 ± 4.0	33.9 ± 6.3
	Fundi	76.4 ± 7.2	45.2 ± 6.4
	Kidneys	47.0 ± 8.5	22.6 ± 5.5

It is of interest to compare the above findings with those encountered in a group of patients with angina pectoris and with coronary occlusion. We again find a high incidence of peripheral, aortic, and renal arteriosclerosis, which is greater than might be expected, as a result of a complicating hypertension present in some of these patients.

One patient with angina pectoris and pernicious anemia, who came to autopsy, had unaltered coronary arteries and aorta. This is an exceptional instance and has been reported in detail elsewhere.[6]

The preponderance of males in these groups is in accordance with common experience.

In Table II the incidence and distribution of peripheral arteriosclerosis and arteriolosclerosis in patients with and without presumptive clinical evidence of coronary disease are listed. While we appreciate the difficulties in the clinical evaluation by palpation of the state of the arterial wall, it would seem that the data are sufficiently accurate satisfactorily to indicate a trend. These observations were made by each of us throughout, so that the subjective errors of interpretation should be uniform.

Thickening of the radial artery was encountered more often than changes in other vessels. This is contrary to pathological experience which teaches that the vessels of the leg and foot are more often and more intensively involved than those of the upper extremity. This is true both for medial calcification, a process which perhaps bears little relation to elevated blood pressure, and for intimal atherosclerosis where such relationship doubtless exists. The low incidence of change of the dorsalis pedis artery in these patients we believe is attributable to the difficulty in adequate interpretation of palpatory findings. Doubtless, atherosclerosis of this artery occurred more frequently than our fingers led us to believe.

The low incidence of changes of the vessels in the ocular fundi, as compared with that reported by other observers, requires a word of explanation. We disregarded minor variations, including only those instances in which we felt certain that the vascular changes were more intense and widespread than could be attributed to the aging process. Briefly, the criteria used were increased tortuosity and light refraction, together with arteriovenous compression, alone or combined with hemorrhage, retinal edema, or degenerative retinal lesions. The changes characteristic of malignant hypertension were not encountered in this group.

It is apparent from Table II that in this group of 90 patients with essential hypertension, clinically ascertainable coronary sclerosis was accompanied by widespread peripheral arteriosclerosis and, in most instances, arteriolar disease as well. No patient was encountered in whom there existed clinical evidence of coronary sclerosis, by our criteria, to the exclusion of evidence of disease in other areas of the vascular bed. The converse of this, however, was not true. There were many patients who apparently had generalized vascular damage without clinical evidence of coronary disease. The pathological data previously given suggest, however, that our clinical criteria were inade-

quate and that in all probability many of these patients had a significant degree of coronary sclerosis.

The above facts, if verified by further observations, may be of clinical value, as regards both diagnosis and prognosis of the cardiac status in patients with essential hypertension.

THE ELECTROCARDIOGRAM

The electrocardiographic abnormalities associated with coronary sclerosis need not be reviewed at this time. Suffice it to say that, in order of frequency, T-wave and R- or S-T changes in significant leads, left axis deviation, intraventricular conduction disturbances, including low voltage of the QRS complexes in all leads, large Q in Lead 3, and of the arrhythmias, extrasystoles, auricular fibrillation, partial or complete heart-block, and auricular flutter, are commonly observed.[7-11] However, certain changes are so often encountered in hypertension that, aside from the question of coronary involvement, it has been suggested[12] that they constitute a typical picture. These changes are left axis deviation, together with increased amplitude of QRS and a tendency for T to be directed oppositely to the major deflection. Master found these alterations in 33 of 152 hypertensive patients. They were for the most part instances of long standing hypertension, and, since the mortality was 40 per cent in three years, it would appear likely that coronary disease was present in many of them.

We have attempted to study the influence of high blood pressure upon the electrocardiogram by statistical analysis of the tracings obtained from two groups of patients, namely, 102 instances of essential hypertension and 87 instances of angina pectoris (Table III). No patient with acute coronary thrombosis was included. The first group was subdivided into patients with and without clinical evidence of coronary sclerosis. The anginal group, most or all of whom presumably had some degree of coronary disease, was subdivided according to the absence or presence of elevated blood pressure. The percentage incidence, with its standard deviation of the mean, has been tabulated for each group with the purpose of demonstrating which changes are significantly influenced by the presence or absence of increased blood pressure and of clinically evident coronary sclerosis. The following changes occurred too infrequently to allow of deduction: bundle-branch block; right axis deviation; inverted T_3; large Q_3; auricular fibrillation; extrasystoles. Table III discloses the following interesting facts.

Left axis deviation: This occurred more often in hypertension with clinical coronary involvement than without, but its incidence was not appreciably influenced by the presence or absence of elevated blood

TABLE III

ELECTROCARDIOGRAPHIC CHANGES IN HYPERTENSIVE PATIENTS WITH AND WITHOUT CLINICAL SYMPTOMS OF CORONARY SCLEROSIS CONTRASTED WITH THE CHANGES IN ANGINA PECTORIS

		HYPERTENSION			ANGINA PECTORIS (87 CASES)	
		WITH CLINICAL COR. SCL.	WITHOUT CLINICAL COR. SCL.	TOTAL	WITHOUT HYPERTENSION	WITH HYPERTENSION
Number of cases		26	76	102	49	38
No change	Per cent	23.0 ± 8.2	28.9 ± 5.1	27.4 ± 4.3	20.4 ± 5.6	13.1 ± 5.3
Left axis deviation	Per cent	57.6 ± 9.6	28.9 ± 5.1	36.2 ± 4.6	36.7 ± 6.8	42.1 ± 8.0
Right axis deviation	Per cent	7.6 ± 5.0	3.9 ± 2.2	4.9 ± 2.0	4.0 ± 2.6	2.6 ± 2.6
T_1 diphasic or inverted	Per cent	34.6 ± 9.0	18.4 ± 4.1	22.5 ± 4.0	22.4 ± 5.9	50.0 ± 8.0
T_2 diphasic or inverted	Per cent	26.9 ± 8.6	18.4 ± 4.1	20.5 ± 3.8	6.1 ± 3.3	44.7 ± 8.0
$T_1 + T_2$ diphasic or inverted	Per cent	23.0 ± 8.2	14.4 ± 3.8	16.6 ± 3.6	20.4 ± 5.6	13.1 ± 5.3
T_3 diphasic or inverted	Per cent	7.6 ± 5.0	3.9 ± 2.2	4.9 ± 2.0	6.1 ± 3.3	23.6 ± 6.9
QRS change (all leads)	Per cent	15.3 ± 7.0	0.0 ± 1.0	3.9 ± 1.7	8.1 ± 3.8	5.2 ± 3.0
Bundle-branch block	Per cent	11.5 ± 6.0	1.3 ± 1.0	3.9 ± 1.7	0.0 ± 1.0	0.0 ± 1.4
Large Q_3 alone	Per cent	0.0 ± 1.7	1.3 ± 1.0	0.9 ± 0.3	4.0 ± 2.6	2.6 ± 2.6
Large Q_3 with other changes	Per cent	11.5 ± 6.0	5.2 ± 2.4	6.8 ± 2.4	4.0 ± 2.6	2.6 ± 2.6
Auricular fibrillation	Per cent	7.6 ± 5.0	2.6 ± 1.7	3.9 ± 1.7	2.0 ± 2.0	13.1 ± 5.3
Extrasystoles	Per cent	15.3 ± 7.0	5.2 ± 2.4	7.8 ± 2.6	12.0 ± 6.6	0.0 ± 1.4

pressure in patients having angina pectoris. This finding is in accord with the experience of Ziskin[13] who could not closely correlate the presence or absence of left axis deviation with the height of the blood pressure or the size of the heart, and concluded that hypertension alone does not produce preponderance. The high incidence of left axis deviation in our series of angina patients with normal blood pressures suggests that coronary disease may well be a factor in its production.

Diphasic or inverted T_1 or T_2: The incidence of these abnormalities was apparently decidedly influenced by the presence of hypertension in our patients. T_1 or T_2 change occurred more frequently in those angina patients with hypertension than in those without; whereas the clinical presence of coronary disease in hypertensive patients increased its incidence but slightly as compared with the rest of the group. While the significance of this finding is not entirely clear, it would indicate caution in the interpretation of such changes, as regards the state of the coronary arteries, in the presence of hypertension.

Combined diphasic or inverted T_1 and T_2: The incidence of this alteration was not increased by the presence of hypertension in the angina group, but was slightly greater in the hypertensive patients with clinical coronary disease. It seems that this change may safely be regarded as indicating the presence of coronary disease in these patients.

In summary, left axis deviation occurs more frequently in the presence of clinical symptoms of coronary sclerosis than in their absence. The presence of increased blood pressure plays little direct part in its production. Isolated changes of either T_1 or T_2 are common in arterial hypertension, and their significance, as regards the diagnosis of coronary artery involvement, is problematical. Changes of T_1 and T_2 together, however, cannot be attributed to the presence of hypertension alone. They probably indicate coronary damage.

SUMMARY

1. Clinically detectable coronary sclerosis occurred in 44.5 ± 3.8 per cent of 155 unselected hypertensive patients, distributed as follows: angina pectoris and cardiac asthma, each 12.2 per cent; electrocardiographic abnormalities only (from a total of 117 tracings) 19.6 per cent; coronary occlusion, 5.1 per cent.

2. In 65 hypertensive patients coming to necropsy, the clinical diagnosis of coronary sclerosis was substantiated in 97 ± 2.8 per cent of the instances in which the diagnosis was made. However, the condition was likewise present in 66.6 ± 8.5 per cent of the remaining patients in whom it was not suspected.

3. Coronary disease in these patients was almost uniformly accompanied by intense vascular changes in other areas of the vascular bed as disclosed by both clinical examination and post-mortem studies. The coronary arteries, however, were occasionally spared in instances of widespread vascular disease.

4. The electrocardiographic findings in this group of patients are contrasted with those encountered in patients having angina pectoris. The influence of uncomplicated hypertension and of coronary sclerosis upon the electrocardiogram is discussed.

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A CASE OF CONGENITAL COMPLETE HEART-BLOCK WITH LABILE VENTRICULAR RATE*

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THE failure of the slowed heart to respond to procedures paralyzing the vagus nerve endings has long been taught as demonstrating an intrinsic heart-block.[1] This has recently been called in question by the careful researches of Gilchrist, who showed that the adult heart with complete auriculoventricular block can accelerate on atropinization provided the drug is given in adequate dosage.[2] This same response to atropine was observed recently in the case of complete heart-block recorded here and regarded as congenital in origin. A similar lability of the ventricular rate characterized the response of this heart to fever, exercise, atropine and epinephrine.

The recent critical and analytical review of Yater, Lyon and McNabb[3] and the inaugural thesis of Archigène[4] serve as the chief guides to the literature on the subject of congenital heart-block. At the present a recapitulation of this material would be untimely. Interest in the case to be described seems to attach as much to the marked lability of the ventricular rate as to the rarity of the condition itself. It will be clear that if the stability of the pulse were to serve as the clue to the diagnosis of complete heart-block in this case, the diagnosis would not have been suspected. Leech[5] in his proved case of congenital block likewise seldom found the same pulse rate at successive examinations. The comparatively high ventricular rate of juvenile block as compared to that of adult block has been commented upon by Clerc and Lévy.[6] This again might serve to divert attention from the possibility of the diagnosis. Gilchrist[7] feels that it is quite likely that at least some of these cases escape detection in childhood on account of the relatively fast ventricular rate. Clerc and Lévy[6] believe that the rapid rate may explain why syncope is so rare in complete block in childhood.

A majority of writers[4, 8-15] have found in cases of congenital complete heart-block that exertion of one form or another produces an acceleration of the heart rate of greater or lesser degree. Lian[16] noted a transient acceleration of the heart and emphasized the importance of taking the rate during fractions of the first minute. Leech[5] described an acceleration to 63 and noted that this response was thought to constitute evidence against the likelihood of there being

*From the Medical Clinic of the Peter Bent Brigham Hospital.

a high degree of block, but a subsequent electrocardiogram showed complete auriculoventricular dissociation. Carter and Howland,[17] McIntosh,[18] Aylward,[19] Anderson[20] and Sclar[21] on the other hand found no change in heart rate to follow exercise.

Campbell and Suzman[15] regard it as likely that chemical changes in the blood, especially the increased carbon dioxide content, are responsible for the increase in rate. That this may not be the entire explanation is attested by the response of some of the hearts of the type under consideration to nervous influences. Thus, whereas Whipham[22] noted no respiratory variation in the ventricular rate, and neither Carter and Howland[17] in their second case nor Fleming and Stevenson[23] in their first case found appreciable changes in the ventricular rate under vagal stimulation, D'Espine and Cottin[24] observed a reflex fall in heart rate from 28 to 24 on ocular pressure.* Leech[5] also found a slight slowing from the oculocardiac reflex. Meyer,[10] peculiarly enough, noted acceleration from 68 to 80 on ocular pressure, but there were extrasystoles.

The effect of atropine on hearts of this sort also has been studied by numerous workers, but unfortunately in many cases the dose given is not recorded.[25, 26] Calandre,[27] Meyer,[10] McIntosh,[18] Davis and Stecher[28] and Brandenberg[29] noted the auricular rate to rise as it does in normal hearts, but they found no essential changes in the ventricular rate. On the other hand Pollak and Hecht,[30] Whipham,[22] Smith,[9] Leech,[5] Aitken,[13] Leaman,[31] and Campbell and Suzman[15] noted ventricular acceleration of variable degree, the maximal rise being observed from twenty to forty minutes after the injection.

That hearts showing congenital complete block can accelerate after epinephrine does not necessarily imply that purely nervous mechanisms are involved. This is amply demonstrated in the work of Cannon and his coworkers, who use the acceleration of the totally denervated heart to detect the presence in the blood stream of minute amounts of adrenin or adrenin-like substances. Thus, acceleration in congenital complete heart-block after epinephrine as described by Meyer,[10] Leech,[5] and Blackford and McGehee[14] is not surprising. The failure of Fleming and Stevenson[23] to produce ventricular acceleration after 0.5 c.c. 1:1,000 epinephrine is probably without significance, for there was no simultaneous auricular acceleration.

The effect of fever in causing a rise in pulse rate has been described by a few authors.[27, 11, 32, 28, 29]

These clinical observations find their counterpart in both anatomical and physiological investigations. Engel,[33] for example, has demonstrated the distribution of nerve fibers in the human heart to Purkinje tissue beyond the auriculoventricular node and the main bundle. Erlanger[34] found that whereas vagus stimulation usually caused no

*Case not electrocardiographically proved to be complete block.

change in the ventricular rate in complete block, in exceptional instances there was a minimal slowing. He also found the ventricular as well as the auricular rates in complete block to increase on stimulation of the accelerator nerve. Hering,[35] as well as Rijhl,[36] found that vagal stimulation caused slowing of the ventricles in experimental complete heart-block. It follows from the above review both clinical and experimental that there are both vagal and accelerator mechanisms which can alter the ventricular rate in complete heart-block.

REPORT OF CASE

The patient was a twelve-year-old schoolboy who was admitted on the medical service of the Peter Bent Brigham Hospital for sore throat and swollen neck glands of three weeks' duration. This began with a sense of irritation in the throat, soreness in the neck, fever, nausea, vomiting, vertigo, and headache. There was also some earache and dysphagia, but these cleared up after a week of bed rest only to return again with marked soreness of the throat and swollen, tender glands on both sides of the neck. Physical examination on admission showed a tall, angular, pale, and poorly nourished boy. The neck glands were large, tender and firm; the pharynx was markedly injected, and all the visible lymphoid tissue was swollen. The temperature was 102.2° F. and the pulse rate 80 beats to the minute. Chief interest centered in the heart. The left border of dullness was percussed 9 cm. to the left of the midsternal line in the fourth intercostal space. The apex impulse was diffuse, and a definite precordial wave, commencing near the nipple and moving toward the sternum with each systole, was caused by the cardiac impact. The first sound at the apex was snapping in quality and was followed by a moderate blowing systolic murmur which was heard well over the entire precordium. There was no cyanosis or clubbing of the fingers. The remainder of the examination, aside from a large scar on the right leg, was negative. On subsequent examination with the heart rate slower the systolic murmur was noted to be loudest in the lower precordium. There was occasionally heard in diastole a dull distant sound particularly well brought out after exercise or with the patient in the left lateral position. In addition there was noted an occasional change in the quality of the first heart sound which became higher pitched and louder.

On admission the white blood cell count was 22,700, the red blood cell count 4,310,000 and the hemoglobin 80 per cent (Sahli). The blood smear showed a differential count of 90 per cent polymorphonuclear leucocytes, 9 per cent lymphocytes, and 1 per cent basophiles. There was a slight "shift to the left." The urine contained the slightest possible trace of albumin by Heller's test, and the sediment was negative.

The temperature dropped to 99° F. by the third day but rose again to 100° F. concomitant with the development of a peritonsillar abscess, which caused the patient very little discomfort and ruptured spontaneously on the fifth day while he was eating lunch. The white blood cell count dropped to 12,700 on the sixth day. The pulse showed marked variations throughout his stay. On the second day it fell to 60, and it then varied around 50 but reached a level of 37 on his seventh day and again rose to 80 on the eighteenth day when the temperature was normal.

Numerous electrocardiographic tracings were taken. One on January 10, 1934, showed complete auriculoventricular dissociation with a ventricular rate of 46.7 and an auricular rate of 82.4. The auricles showed sinus arrhythmia. The complexes were upright in all leads. Tracings were not obtained at the times the heart rate

was 80 per minute. A roentgen ray film of the heart showed no cardiac enlargement or abnormality in contour other than a rather straight left border. The hilus shadows were slightly exaggerated. The diagnosis of congenital complete heart-block with probable interventricular septal defect was made.

The antecedent history of the patient was rather interesting. He weighed seven pounds at birth, and no cyanosis was noted at that time. He developed normally and was weaned at eleven months. At the age of two weeks he was examined by Dr. Karlton G. Percy of the Brookline (Mass.) Health Unit. He found the radial and apical rates to be 72 beats to the minute and noted a soft blowing systolic murmur heard best at the pulmonic area. His diagnosis was congenital heart disease. At the age of four the patient sustained extensive burns of his right leg; he was treated for this at the Children's Hospital with skin grafts, and he was followed at that institution as a case of congenital heart-block. He had pneumonia at the age of eight years and several attacks of asthma for which he was tested with negative findings. He gave no history of diphtheria, scarlet fever, rheumatic fever, or chorea. He had always been somewhat underweight and sickly, falling two years behind his classmates, but he was able to enter into practically all their activities. He never had syncopal or convulsive attacks. It is of interest that when treated at the Children's Hospital his pulse on admission was 135, then ranged between 53 and 90, the usual pulse being rather constantly at a level of 60.

During convalescence at the Peter Bent Brigham Hospital numerous studies were carried out. These included study of the effects of epinephrine, atropine, exercise, vagal pressure, carotid sinus pressure and ocular pressure. The ventricular as well as the auricular rates were accelerated after epinephine, atropine, and exercise. The ventricular rate rose from 45.2 to a maximum of 74.3 beats per minute twenty-three

TABLE I

EFFECT OF EPINEPHRINE ON BLOOD PRESSURE, CIRCULATION TIME, AURICULAR AND VENTRICULAR RATES*

ELECTRO-CARDIOGRAM	TIME	BLOOD PRESSURE	CIRCULATION TIME	AURICULAR RATE	VENTRICULAR RATE
1	Control (see upper tracing Fig. 1).	145/60	–	87.7	45.2
2	Determination of circulation time (0.25 c.c. 2 per cent sodium cyanide).	–	13 seconds	88.2	44.9
3	Five minutes after subcutaneous injection of 0.5 c.c. 1:1,000 epinephrine.	170/65	–	91.2	46.8
4	Seven minutes after injection.	170/60	–	96.6	47.4
5	Determination of circulation time (0.20 c.c. 2 per cent sodium cyanide).	–	9 seconds	100.3	51.4
6	Twenty minutes after injection (frequent extrasystoles).	180/60	–	117.6	62.6
7	Twenty-three minutes after injection. (See lower tracing Fig. 1.)	–	–	131.0	74.3
8	Twenty-six minutes after injection.	202/56	–	124.1	63.4

*I wish to thank Dr. M. A. Schnither for assistance in carrying out this experiment.

minutes after the subcutaneous injection of 0.5 c.c. 1:1,000 epinephrine (Table I). At this time there were frequent extrasystoles, but the rate was counted in a strip in which there were no extrasystoles (Fig. 1). There was no change in the grade of block. The circulation time as determined by the sodium cyanide method fell from thirteen seconds to nine seconds seventeen minutes after the injection of epinephrine.

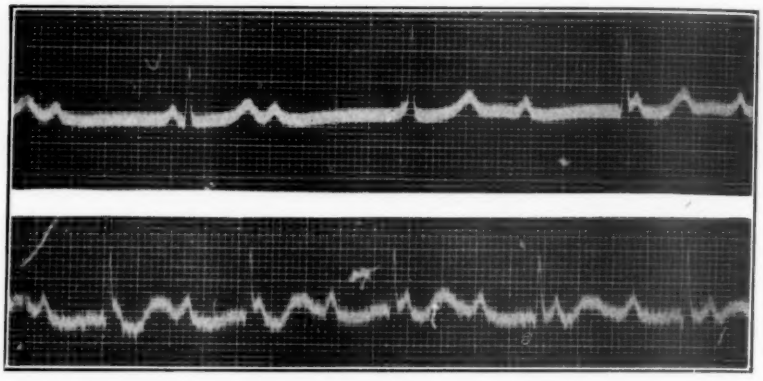

Fig. 1.—Electrocardiographic tracings taken before and twenty-three minutes after the subcutaneous injection of 0.5 c.c. 1:1000 epinephrine. Upper tracing (control) shows auricular rate 87.7 per minute and ventricular rate 45.2 per minute. Lower tracing shows auricular rate 131.0 and ventricular rate 74.3 per minute in a strip in which no extrasystoles are present. Both tracings are from Lead II.

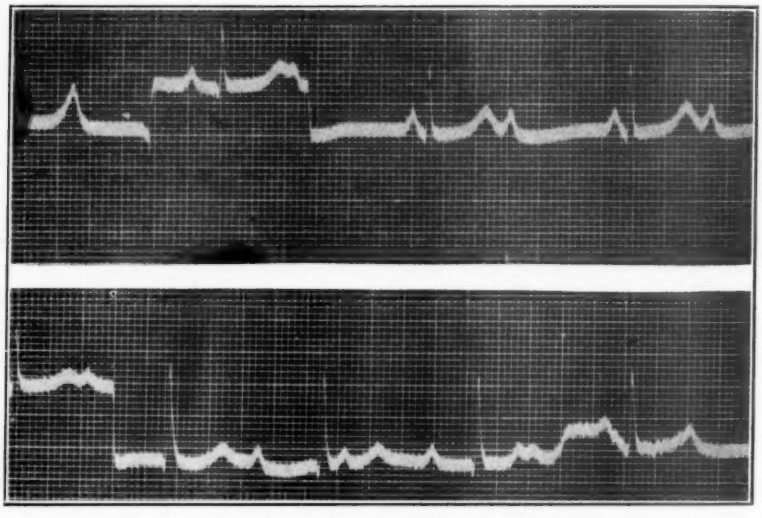

Fig. 2.—Electrocardiographic tracings taken before and one hour after the subcutaneous injection of 1 mg. of atropine sulphate. Upper tracing (control) taken from Lead II shows auricular rate 88.9 and ventricular rate 46.8 per minute. Lower tracing taken from Lead III shows auricular rate 107.9 and ventricular rate 59.1 per minute.

The ventricular rate rose from 46.8 to 59.1 beats per minute one hour after the subcutaneous injection of one milligram of atropine sulphate (Table II, Fig. 2). There is reason to believe that the rate might have been counted at a still higher level, if counts had been made at intervals during the first hour (see above). Exercise consisting of hopping alternately on each leg for three minutes caused a

slight transient acceleration of the heart rate, most apparent when the rate was counted each quarter-minute. During the first two quarter-minutes the calculated rates rose from 50 beats per minute to 56 beats per minute (Table III). While strong carotid sinus pressure or pressure on either vagus nerve lower down in the neck produced essentially no change in the rate, ocular pressure produced a slowing amounting to four beats per minute. There was no respiratory change in the ventricular rate.

TABLE II

EFFECT OF ATROPINE ON AURICULAR AND VENTRICULAR RATES

ELECTROCARDIOGRAM	TIME	AURICULAR RATE	VENTRICULAR RATE
1	Before injection (see upper tracing Fig. 2).	88.9	46.9
2	One hour after subcutaneous injection of 1 mg. atropine sulphate. (See lower tracing Fig. 2.)	107.4	59.1
3	Two hours after same.	68.3	42.8
4	Three hours after same.	63.7	34.8

TABLE III

EFFECT OF EXERCISE, CAROTID SINUS PRESSURE, VAGAL PRESSURE AND OCULAR PRESSURE ON THE HEART RATE

	RATE BEFORE EXERCISE	RATE BEFORE CAROTID SINUS PRESSURE		RATE BEFORE VAGAL PRESSURE		RATE BEFORE OCULAR PRESSURE	
		Right	Left	Right	Left	Right	Left
First quarter minute	13	11	11	12	12	12	12
Second quarter minute	12	11	11	12	12	12	12
Third quarter minute	13	11	11	12	12	12	11
Fourth quarter minute	12	12	11	12	12	12	11
	RATE AFTER EXERCISE	RATE DURING CAROTID SINUS PRESSURE		RATE DURING VAGAL PRESSURE		RATE DURING OCULAR PRESSURE	
		Right	Left	Right	Left	Right	Left
First quarter minute	14	11	11	12	12	11	11
Second quarter minute	14	12	11	12	12	11	10
Third quarter minute	12	11	11	12	11	11	10
Fourth quarter minute	11	12	11	13	12	–	–
Fifth quarter minute	12	–	–	–	–	–	–
Sixth quarter minute	12	–	–	–	–	–	–
Seventh quarter minute	13	–	–	–	–	–	–
Eighth quarter minute	13	–	–	–	–	–	–

SUMMARY

A case is described of congenital complete heart-block with probable interventricular septal defect, seen during an attack of acute tonsillitis. The ventricular rate varied spontaneously and with fever, exercise, ocular pressure, and the administration of atropine and epinephrine. The subject of the lability of the ventricular rate in congenital complete heart-block is discussed.

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Department of Clinical Reports

INTRAPERICARDIAL RUPTURE OF AORTA

Report of Two Cases

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NO ATTEMPT will be made to review the literature on this very interesting subject. A review of the first case reported makes one wonder how early in life degenerative changes may be expected. It is unfortunate that the clinical study of this patient is so limited, but he was not admitted to the hospital, as the seriousness of his illness was not suspected.

Case 1.—G. H. H., white male, aged nineteen years, well-developed young athlete and student in the Citizens' Military Training Camp, Fort Snelling, Minnesota, August, 1932. He was an excellent tennis player and had reached the semi-finals in doubles and singles in the C. M. T. C. tournament when he was forced to withdraw because of very severe precordial pain on August 21, 1932. This severe pain was of short duration, but there was a persistent feeling of uneasiness with anxiety that was progressive up to the fatal termination.

His mother and father both have arterial hypertension.

Present Illness: August 23, 1932, about 7 P.M., while in a stooping position washing his clothes, he was conscious of a sharp, cracking sensation in his chest. This was, however, not complained of until one hour later when he complained of pain in his right chest, dyspnea and anxiety. Examination by a doctor showed temperature normal, pulse 80, respiration 22. During the night he was uncomfortable, slept very little, and the pain in right chest continued. He remained in quarters August 24 with the same symptoms and pain prevailing. Appetite was nil. He again spent a very restless, anxious night. On the morning of August 25 he was up by 6 A.M., and still complained of pain in his chest. He was instructed to remain in his barracks for the day, where at 8:55 A.M. he was found lying across his bed unconscious, after having taken a gun out of a rack for another student. There was marked cyanosis of face and hands, and respiration was labored. He was soon seen by several of the Camp physicians and at 9 A.M. was pronounced dead. Apparently this exertion completed the rupture of the aorta, with the resultant intrapericardial hemorrhage.

Personal History: He had the usual childhood diseases without complications. Had never had any prolonged illness. No operation of any kind. Always healthy, was an excellent athlete, playing baseball, basket-ball, football and tennis. Denied venereal diseases.

An autopsy done by Major T. W. O'Brien, M. C., showed the following: "The pericardium is distended and filled with blood (about 200 c.c. in amount) due to a rupture of the ascending aorta. The heart is in firm contraction, normal in size with a well-developed left ventricle. There is a rupture in the ascending

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aorta, extending in an irregular, longitudinal direction upward from a point just above the right coronary artery for a distance of 3 inches. The tear in the intima was definitely older than that in the adventitia, which apparently occurred several days later after the blood had dissected posteriorly between the intima and adventitia. The rupture in the adventitia was distal to the rent in the intima. From the appearance of the dissecting hemorrhage one would believe it to be probably several days old. No other pathological lesion of importance was found elsewhere."

Microscopic Report: (Made by Major P. E. McNabb, Medical Corps.) "Sections made through the aorta at a point some distance from the rupture show a mild separation of the tissue elements in the media. The adventitia is thickened both by increased fibrous tissue and by edema. There is no recent in-

Fig. 1.

flammatory reaction in the region. The section taken from near the point of rupture shows degeneration in the media, but the adventitia is widely separated from the media by a massive hemorrhagic infiltration. This appears to be of different ages, and in many areas the clot contains numerous leucocytes and a large amount of blood pigment. In the adventitia there is both diffuse and localized infiltration of leucocytes. The most conspicuous change, however, occurs in the endothelium of the blood vessels. One of the sections shows a longitudinally directed vessel in which the endothelium is remarkably swollen, proliferating, and in some areas appears to have two or three rows of cuboidal shaped cells. Some of these enlarged endothelial cells are detached into the lumen of the vessel."

CASE 2.—J. W. L., white male, aged fifty-five years, was admitted to Fitzsimons General Hospital March 27, 1934, with the following history:

Symptoms and Complaints: Coughing and expectorating blood. Face, lips and finger tips cyanotic. Pain, severe, in the left chest; weakness and cardiac distress on respiratory movement. Marked insomnia for two days.

Present Illness: The patient was in good health until March 25, 1934, when he was defrosting a refrigerator and was seized with a sudden, severe, cardiac pain, as if he had been shot. Respiration increased this pain, and he had to be assisted to a chair where he soon fainted and fell to the floor. When he revived he felt weak and cold, and still had the severe pain in the left chest. The family physician soon was called in, and he felt there was some coronary disease. His general condition remained much the same until he was admitted to this hospital on the afternoon of March 27, 1934.

Personal History: Herniotomy, left, 1919, with recurrence several years later. Hemorrhoidectomy and tonsillectomy, 1927. Second repair of hernia, left, January, 1934. The last operation was apparently successful and recovery was uneventful. Always enjoyed good health; no change in weight; denied venereal diseases (Wassermann negative at this hospital in 1927), and family history was essentially negative.

Condition on Admission: Pulse 108, temperature 99° F., respiration 26. A well-developed, white male with good nutrition, weighing about 175 pounds. Face, lips and finger tips cyanotic. Coughing moderate, with some expectoration of blood. Pupils equal in size, active to light. Reflexes considered as normal. Blood pressure 190/120 mm. White blood count 14,000 with 89 per cent of polymorphonuclears.

An x-ray film made soon after admission was reported as follows: "Bedside x-ray examination of the chest shows the thorax negative. Trachea lies slightly to the right of the midline. Cardiac shadow is somewhat horizontal in shape and appears slightly enlarged to the left and right. There appears to be a considerable tortuosity of the thoracic aorta. A mottled, uneven clouding in the basal portion of the right lung is suggestive of a lung infarct. This lung is otherwise clear. The left lung is essentially negative."

An electrocardiogram made March 29 showed the following: "Auricular rate 107; ventricular rate 107; rhythm regular; left axis deviation; P_2 is diphasic; P-R interval is 0.10 sec.; QRS slurred in Lead III; S-T elevated (marked) in Leads I and II; depressed in Lead III; T-wave inverted, Lead III. The findings in this case suggest acute coronary thrombosis with severe myocardial damage."

The patient's general condition remained about the same while he was in the hospital until the morning of March 31, 1934. While he was eating his breakfast, the nurse left the room for a few minutes, and on her return she found him dead.

The autopsy, made by Major H. P. Sawyer, M. C., follows: "The heart is huge and on palpation appears to be solid. The pericardium is so thick that one cannot see the color of the blood through it. On opening the pericardium a huge clot is found surrounding the entire heart, extending up to the great vessels and about 900 c.c. in amount. The pericardium at about the auriculoventricular septum shows a line of old visceroparietal adhesions. Above this old line the clot seems older and is firmer and more fibrous. The lower portion of the clot is more recent and more fluid. The right heart is fairly normal, the muscle pale but firm. The valves are all normal. The right ventricle appears as if plastered over the right side of the globular, hypertrophied left ventricle. The latter is about 2.5 cm. in thickness. The mitral valves appear competent. Following up the aorta about 3 cm. above the sinuses of Valsalva there is a long rupture which is directed upward and a little to the right. The aorta shows a moderate sclerosis from the summit of the arch down to the bifurcation, but at the rupture there is very little sclerosis. At the point of rupture the wall is

a little thinner than elsewhere. There is a noticeable fatty infiltration of the media in the sclerotic areas. The coronaries show a moderate amount of sclerosis, but there is no occlusion. The impression is that a small rupture occurred first on exertion, the resulting hemorrhage into the pericardial sac being confined for the time being to the upper third of the sac by the line of adhesions along the auriculoventricular septum. Later the primary rupture enlarged, due to pressure, the retaining line of adhesions gave way, and the entire sac filled to extreme distention."

Fig. 2.

Microscopic Report of Aorta: "Sections made at the site of rupture show the elastic fibers of the media, which are markedly decreased in all sections, are still more infrequent as the line of rupture is approached. Both elastica interna and externa are either totally absent or so thin as to be unrecognizable. There is a noticeable infiltration of the media with fat and a definite degeneration of all the medial elements. There also appears a large, misplaced branch of the vasa vasorum which occupies the medial portion of the section and in one place bulges the interna markedly. The tear in the artery traverses the vascular appearing space, which practically halves the thickness of the wall."

This second case is especially interesting in that the recorded damage as shown by the electrocardiograph resembled that of acute coronary thrombosis. It is believed that this may have been due to the pressure of the tensely distended pericardial sac upon the coronary branches, resulting in ischemia of the heart muscle.

These cases are reported chiefly to show that degenerative changes of the cardiovascular system may be present in youth. It is possible that they are much more prevalent than is believed. In the case of the C.M.T.C. student the violent exercise apparently caused death in a person who possibly might have lived out the average span of life had he not been such an ardent participant in strenuous sports.

Society Transactions

AMERICAN HEART ASSOCIATION, 1934

THE tenth annual scientific session of the American Heart Association was held on June 12, 1934, at the Hotel Cleveland, Cleveland, Ohio, with Dr. Harold E. B. Pardee as presiding officer. The following program was presented.

Program

Pathology of Coronary Sclerosis. Timothy Leary, M.D., Boston, Mass. See page 328.

Coronary Spasm as a Possible Factor in Producing Sudden Death. Timothy Leary, M.D., Boston, Mass. See page 338.

Coronary Arteriosclerosis, Coronary Thrombosis, and the Resulting Myocardial Changes. I. Anatomical Lesions. Otto Saphir, M.D., Walter S. Priest, M.D., Walter W. Hamburger, M.D., and Louis N. Katz, M.D., Chicago, Ill. To be published in a later issue of the AMERICAN HEART JOURNAL.

A Clinical and Pathological Study of Coronary Sclerosis: Its Incidence in Hypertension and Angina Pectoris. F. R. Nuzum, M.D., A. H. Elliott, M.D., and R. D. Evans, M.D., Santa Barbara, Calif. See page 367.

The Relation of Coronary Arteriosclerosis to Auricular Fibrillation With Special Reference to the Term "Arteriosclerotic Heart Disease." Morton G. Brown, M.D., and Samuel A. Levine, M.D., Boston, Mass.

ABSTRACT

An analysis was made of all cases with auricular fibrillation which came to postmortem examination at the Peter Bent Brigham Hospital, exclusive of those with known rheumatic valvular disease. Significant disease of the coronary arteries, although fairly frequent among those with hypertension, was not usually the sole factor in the development of permanent fibrillation. Hypertension was an etiological factor in 63.8 per cent of the cases with permanent fibrillation, and in 67.8 per cent of those with transient fibrillation. Evidence is presented that marked peripheral arteriosclerosis of itself need be no indication that the coronary arteries are sclerosed, or that the efficiency of the heart is in any way altered. From this, we therefore suggest that the term "arteriosclerotic heart disease" should be given up entirely or clarified in its expression.

The Relation of Arteriosclerosis to Hypertrophy of the Heart. James G. Carr, M.D., Chicago, Ill.

ABSTRACT

This paper is based upon a study of 351 autopsy reports from the Cook County Hospital. These reports are studied in four groups: (1) a group with cardiac hypertrophy in which cardiac disease was the cause of death; (2) a group in which cardiac hypertrophy was present as an incidental finding; (3) a group in which severe coronary sclerosis was accepted as the principal disease; (4) a group in which generalized arteriosclerosis was incidental, in a very few of these cases the arteriosclerosis was regarded as the principal disease. Group 4 includes no reports considered in the other groups. No reports are included in which the cardiac enlarge-

ment could be attributed to valvular or renal disease. An attempt is made to evaluate arteriosclerosis, general or especially pronounced in the coronary vessels, as a factor in the production of cardiac hypertrophy. Thus far the study does not support the view that arteriosclerosis is a cause of cardiac hypertrophy.

Arteriosclerotic Heart Disease: Coronary Thrombosis and Its Effect on the Size of the Heart. Emmet F. Horine, M.D., and Morris M. Weiss, M.D., Louisville, Ky.

ABSTRACT

Statements have been made that coronary thrombosis of itself may produce cardiac enlargement. Patients with arteriosclerotic heart disease and normal sized hearts who developed coronary thrombosis were followed for varying intervals of years. None developed cardiac enlargement. Heart-block, arteriosclerotic in origin, did not produce cardiac enlargement. Autopsy studies and a brief summary of pertinent literature are included.

Arteriosclerotic Heart Disease in Diabetes. H. F. Root, M.D., and T. P. Sharkey, M.D., Boston, Mass.

ABSTRACT

The frequency and severity of arteriosclerotic heart disease as demonstrated by autopsy examinations at the New England Deaconess Hospital were correlated with the clinical records, special attention being given to the etiological factors of hypertension, obesity, and duration of diabetes. One-half the patients had had hypertension. The symptomatology and clinical course of the cardiac cases were characteristically those of insufficiency of the coronary circulation, with a high incidence of acute coronary thrombosis as a cause of death. The severity of coronary disease was greater in the hypertensive group, but the incidence of arteriosclerotic gangrene of the feet was less affected by hypertension. Absence of marked hypertrophy of the heart, even in the presence of hypertension together with a high incidence of myocardial degeneration, was noted. Distinction between arteriolar sclerosis and large vessel sclerosis was not clear-cut because of the coexistence of both types. The evidence indicates that arteriosclerosis is unimportant as a cause of diabetes, but the development of arteriosclerotic heart disease in diabetic patients is excessive.

Valvular Atherosclerosis. Sylvester McGinn, M.D., and Paul D. White, M.D., Boston, Mass. To be published in a later issue of the AMERICAN HEART JOURNAL.

Coronary Arteriosclerosis, Coronary Thrombosis and the Resulting Myocardial Changes. II. An Evaluation of the Clinical Pictures Including the Electrocardiographic Records Based on the Anatomical Findings. Walter S. Priest, M.D., Walter W. Hamburger, M.D., Louis N. Katz, M.D., and Otto Saphir, M.D., Chicago, Ill. To be published in a later issue of the AMERICAN HEART JOURNAL.

Significance of the Coronary Circulation in Arteriosclerotic Heart Disease. Fred. M. Smith, M.D., W. D. Paul, M.D., Iowa City, and H. W. Rathe, M.D., Waverly, Iowa.

ABSTRACT

This report is based on the study of approximately 400 cases of arteriosclerotic heart disease in which there was a significant involvement of the coronary arteries. Forty-five of these cases came to necropsy. The progress of the cardiac disability was analyzed with reference to the vague clinical manifestations and their relationship to possible disturbance in the coronary circulation. We have been par-

ticularly interested in the incidence of suspected and unmistakable coronary accidents, the significance of paroxysmal dyspnea and the relationship between angina of effort and coronary occlusion. Most of these patients were studied electrocardiographically, and many had serial curves. This study emphasizes the importance of constantly bearing in mind the status of the coronary circulation in arteriosclerotic heart disease. In the patients who came to necropsy there was, in general, a close correlation between the clinical interpretation and the pathological findings.

Mechanism of Pain Production in Angina Pectoris. Louis N. Katz, M.D., Chicago, Ill. See page 322.

Anginal Pain and Coronary Disease: A Clinical and Pathological Study of 500 Cases. Kenneth B. Turner, M.D., Howard G. Bruenn, M.D., and Robert L. Levy, M.D., New York, N. Y.

ABSTRACT

This series of cases has been analyzed with cardiac pain as the central point of interest, in an attempt to correlate the clinical aspects and the pathological anatomy. Various etiological types and degrees of coronary artery disease have been considered. Such factors as the location of the lesions, character and extent of myocardial involvement, associated clinical and pathological states and causes of death are discussed. The circumstances which favor the occurrence of anginal pain are described.

The Relation of Symptoms of Cardiac Infarction to the Pathological Findings. Nathan S. Davis, III, M.D., Chicago, Ill.

ABSTRACT

An analysis of the records of 77 successive cases of cardiac infarction has been made. Pain was present in about 48 per cent, absent in about 33 per cent, and in 18 per cent there was no history. In the group with pain, epigastric pain was present in about 14 per cent, nocturnal angina in 8 per cent, and about 35 per cent had had previous anginal attacks. Nocturnal dyspnea, paroxysmal dyspnea, and congestive heart failure were more common in the group without pain, as were also cardiac dilatation and cardiac aneurysm. Occlusion of the circumflex branch of the left coronary artery was found most often in those patients without history; occlusion of the descending branch in those with and without pain. Stenosis and occlusion in one branch or stenosis in one and occlusion in another occurred most often in those with pain, least often in those without. Myomalacia, hemorrhagic, irregular and multiple areas of infarction are relatively more common in those with pain; recent and ancient fibrosis, anemic and circumscribed areas of infarction in those without pain.

Factors Which Obscure Electrocardiographic Diagnosis and Localization of Acute Myocardial Infarction, and Recent Observations Permitting Greater Accuracy of Diagnosis. A. R. Barnes, M.D., Rochester, Minn.

ABSTRACT

Analysis of a large series of cases of acute myocardial infarction reveals several factors which interfere with the development of typical electrocardiographic changes. These factors are discussed and illustrated. The importance of observing the electrocardiographic changes in the initial ventricular complex, and especially the value of the combined study of the initial and final ventricular complexes, is stressed. The electrocardiographic pattern which may develop when acute coronary occlusion is complicated by pericarditis is pointed out. The interpretation of minimal electro-

cardiographic changes of infarction is discussed. The supplementary information obtained under such conditions by the use of anteroposterior thoracic leads is illustrated.

Localization of Cardiac Infarcts According to Component Ventricular Muscles. Jane Sands Robb, M.D., J. G. Fred Hiss, M.D., and Robert C. Robb, Sc.D., Syracuse, N. Y. See page 287.

Electrocardiograms in Coronary Sclerosis and Occlusion. Howard B. Sprague, M.D., and Edward S. Orgain, M.D., Boston, Mass.

ABSTRACT

This study correlates the electrocardiograms taken during the course of acute coronary occlusion with the pathological findings. A similar correlation is made in a series with diffuse myocardial change with or without evidence of old myocardial infarct. A third group has been studied in which the autopsy findings revealed advanced coronary sclerosis but in which the electrocardiographic findings were equivocal. Electrocardiograms of patients with coronary arteriosclerosis but without cardiac infarction may provide very indefinite evidence of the severity of the process.

Changes in the Electrocardiogram Resulting From Induced Attacks of Angina Pectoris. Merritt B. Whitten, M.D., and James H. Herndon, M.D., Dallas, Texas.

ABSTRACT

Electrocardiograms were taken on a number of patients before and during attacks of angina pectoris induced by exercise. Striking changes in the electrocardiogram, especially in the Q-wave, RS-T interval and T-wave, were observed in a number of the cases. Others showed only slight changes in the Q- and T-waves and RS-T interval. Control patients were studied to determine how slight a change in the various waves and intervals of the electrocardiogram might be considered significant following exercise similar to that producing the anginal attacks. Control cases included (1) patients with typical history of angina pectoris, but in which we failed to precipitate anginal pain on exercise, (2) patients exhibiting heart disease other than that involving the coronary arteries, and (3) patients with apparently no organic heart disease. A study of the electrocardiograms in these control cases seemed to indicate that slight changes in the electrocardiogram occur with exercise even in the absence of angina pectoris.

Observations on Prognosis in Angina Pectoris. A. M. Wedd, M.D., and R. E. Smith, M.D., Clifton Springs, N. Y.

ABSTRACT

The paper is based on the records of 165 cases of angina of effort, seen in a clinic in which arteriosclerotic heart disease is the predominant type. The influence of hypertension, obesity, familial vascular disease, and certain miscellaneous factors has been considered. Electrocardiograms were available in most cases but were found of no value for prognosis. One-third of these patients died suddenly, and over one-half died of coronary occlusion. The duration of life in this series was greater than is usually anticipated. While prognosis in the individual case must always be uncertain, because of the long duration and the late ages of onset and death compared with life expectancy, the anginal syndrome does not stand out as a serious complication of arteriosclerotic heart disease.

Observations on the Pathology and Pharmacology of Syncope and Sudden Death in Coronary Disease. M. H. Nathanson, M.D., Minneapolis, Minn.

ABSTRACT

An analysis of 142 necropsy records of patients who had had coronary disease terminating in sudden death indicated that a structural basis for the sudden death is infrequent. The effect of drugs upon the two mechanisms within the heart which may cause a sudden cessation of circulation, i.e., ventricular fibrillation and ventricular standstill, was studied in human subjects. The cardiac standstill induced by carotid sinus pressure could be prevented by a large number of compounds, all related in structure to epinephrine. The preponderance of evidence indicates that ventricular fibrillation is usually the underlying mechanism in sudden cardiac death. Ventricular rhythms of a prefibrillation type were induced by intravenous injection of epinephrine and the effect of various drugs investigated. Quinidine prevented the development of these rhythms in ten subjects. The action of ergotamine, potassium salts, sodium amytal and acetyl-B methylcholin was studied in a smaller group of cases. By utilizing the carotid sinus reflex, quinidine was found to possess a vagoparetic action and thus would also have a tendency to prevent vagal inhibition of the heart.

Treatment of Various Forms of Arteriosclerotic Heart Disease by Means of Total Ablation of the Normal Thyroid Gland. David Davis, M.D., A. A. Weinstein, M.D., J. E. F. Riseman, M.D., and H. L. Blumgart, M.D., Boston, Mass. To be published in a later issue of the AMERICAN HEART JOURNAL.

Theophyllin in the Treatment of Arteriosclerotic Heart Disease. Fred M. Smith, M.D., W. D. Paul, M.D., Iowa City, and H. W. Rathe, M.D., Waverly, Iowa.

ABSTRACT

Theophyllin in the form of theophyllin ethylendiamin has been employed at the University Hospital for the past seven years in the treatment of arteriosclerotic heart disease. This medication was often continued after the patient was discharged from the hospital, and in certain instances it was taken over a period of several weeks or months. Frequently these patients reported that they were progressing very satisfactorily, but soon after the drug was discontinued the symptoms returned. This study also includes observations on a series of approximately 100 patients who were not hospitalized. In the majority of these, theophyllin was the only cardiac drug employed. This series consisted of patients presenting varying degrees of dyspnea including the paroxysmal type (some with extensive edema), angina of effort, and coronary occlusion. Our observations have convinced us that theophyllin is a valuable remedy in the treatment of arteriosclerotic heart disease.

Tolerance to Digitalis in Patients With Normal Hearts and in Those With Arteriosclerotic Heart Disease. Thomas M. McMillan, M.D., Samuel Bellet, M.D., and William E. Robertson, M.D., Philadelphia, Pa. To be published in a later issue of the AMERICAN HEART JOURNAL.

(Papers read by title)

The Chemistry and Morphology of Normal and Atheromatous Aortas. Pearl M. Zeek, M.D., Cincinnati, Ohio.

ABSTRACT

Over 20 sections on nonsyphilitic aortas, ranging from the normal to markedly sclerotic ones, have been analyzed quantitatively for lipoids, a small portion of each also being sectioned for microscopic study, and lantern slides prepared. The lipoid

percentages include those for total cholesterol, free cholesterol, cholesterol esters, fatty acids, and lecithin, the methods used being essentially those of Dr. Bloor of Rochester, N. Y. Graphs are being drawn to show the relationship between the degree of atheroma and the percentages of the various lipoid substances.

Arteriolar Lesions of Skeletal Muscle in Hypertension. R. W. Scott, M.D., David P. Seecof, M.D., and A. A. Hill, M.D., Cleveland, Ohio. See page 355.

How Often Is Arteriosclerotic Heart Disease an Isolated Arteriosclerotic Manifestation? Edward W. Hollingsworth, M.D., and W. L. McNamara, M.D., Hines, Ill.

ABSTRACT

The diagnosis of arteriosclerotic heart disease was considered established when there were the usual findings of myocardial disease and when syphilis, rheumatic fever, hypertension and sepsis could be ruled out. Slides of the various tissues were examined and changes noted in the thickness of the walls of the arteries, which were divided roughly into large and small. The dividing point in our classification was about 75 microns. Because of distortion in sections, including collapse and shrinkage, the ratio between wall and lumen was not employed. Routine formalin fixation was employed. In practically every case there was sclerosis in organs other than the heart. In the heart itself the large vessels were more frequently and more severely affected than the small. Both large and small kidney vessels were affected in practically every case, and about equally; the same applies to the spleen. The vessels of the other organs—adrenals, pancreas, brain, and lungs—in the order named, were less often and less severely involved. These findings are, in general, in agreement with those of other writers, excepting that there was no marked difference between frequency or severity of involvement in small and large arteries.

Observations on the Clinical Course of Arteriosclerotic Auricular Fibrillation. Louis F. Bishop, M.D., and Louis F. Bishop, Jr., M.D., New York, N. Y.

ABSTRACT

Sixty-eight patients with arteriosclerotic auricular fibrillation who had been followed in practice for a number of years were studied. Paroxysmal and chronic fibrillation are separately considered. A subdivision is made into arteriosclerosis with and without hypertension. Age, sex, symptomatology, and mode of treatment with particular regard to digitalis and exercise, are reviewed. The clinical course of these patients is analyzed as to their physical activity, occurrence of embolism, onset of congestive failure, and duration of life.

The Value of the Electrocardiogram in Interpreting Coronary Disease. Louis N. Katz, M.D., Anne Bohning, M.D., Chicago, Ill., and Harry Landt, M.D., Cincinnati, Ohio.

ABSTRACT

In only five of more than 100 cases diagnosed clinically as advanced coronary sclerosis were the four leads found to be normal, but never, as yet, after a recent coronary occlusion (more than 50 cases). In some of these latter the characteristic changes appeared only in Lead IV. The use of frequent serial four-lead records has been of assistance in differentiating between anginal attacks and myocardial infarction, and in determining whether the coronary sclerotic process is rapidly progressive or relatively stationary. Exercise was found to produce changes in the four leads in proportion to the degree of impairment of the coronary circulation.

An analysis of the standard three leads of our records of recent coronary occlusion shows that mixed T types often occur and occasionally the changes in Lead I and Lead III are in the same direction. These types fall into: (1) the indeterminate, (2) T_a and (3) T_p types. Positive coronary T-waves may be the dominant alteration on occasion instead of the negative coronary T-wave. In a small series of cases (seven) checked by autopsy, Lead IV was useful in differentiating anterior from posterior infarcts, even when the ordinary leads were misleading or not characteristic.

The Effect of Theophyllin Ethylendiamin on Experimentally Induced Cardiac Infarction in the Dog. W. M. Fowler, M.D., H. M. Hurewitz, M.D., and Fred M. Smith, M.D., Iowa City, Iowa.

ABSTRACT

In perfusion experiments on the isolated heart of the rabbit theophyllin ethylendiamin produced a far greater and more consistent increase in the rate of coronary flow than did any of the various drugs tested. This drug was put to a more decisive test by observing its effect on the infarct produced by the ligation of a coronary artery in the dog. Observations were made during the initial stage of the infarction and after an interval of three weeks. In the first series of experiments a coronary vessel was ligated, and after the appearance of the distal area of cyanosis the drug was administered intravenously. This was followed by a decided reduction in the extent and degree of cyanosis, and in certain instances resulted in almost complete restoration of the original color. The drug was then given at daily intervals to a series of animals after the ligation of a coronary artery. These animals were sacrificed after an interval of three weeks, which, in view of the findings, allowed ample time for the restoration of the circulation to the area of infarction. This area was greatly diminished in these animals as compared to that in the control series which did not receive medication and in which a corresponding vessel was ligated at the same level. These results indicate that theophyllin ethylendiamin promotes the development of an extensive collateral circulation.

Discussion

Discussion of the papers on "Pathology of Coronary Sclerosis" and "Coronary Spasm as a Possible Factor in Producing Sudden Death" by Dr. Leary.

Dr. James B. Herrick, Chicago, Ill.—We are to be congratulated on having the opportunity of listening to these stimulating papers. The one pathological condition which is commonly found in coronary thrombosis is sclerosis of the coronary artery. Dr. Leary is trying to tell us what is the cause of this sclerosis and what is its nature. Possibly he can some day tell us how we may prevent it.

His work has at least an indirect bearing on the question of the frequency, or the possible increased frequency, of coronary thrombosis. The question is asked many times, "Is this disease increasing in frequency?" We know that, because more people are living to the coronary age, more cases are seen than formerly. Personally I believe that the special reason why the disease is increasing in frequency, or seems to be, is because it is today recognized by the clinician and by the pathologist. A few years ago it was overlooked by both. At any rate in looking over the literature one finds as far back as the time of Jenner and Parry that numerous cases of coronary thrombosis are down in the records as angina. Just the other day Dr. Levy and his coworkers showed that since the disease was recognized clinically, statistics reveal a sharp increase in the number of cases reported by the clinician and the pathologist.

I hope that Dr. Leary, later perhaps, can tell us what is the real cause of thrombosis, and its relation to the seeming increase in the disease. Statistics from

Germany and from other countries are by no means convincing that thrombosis has increased enormously. Some of the German writers are correct when they say that we must have better and more uniform standards of comparison than we have today with longer periods of observation before we can say to what extent thrombosis has increased.

One other point, and that is with regard to the sudden onset of coronary thrombosis. I am not referring to the cases of so-called gradual or chronic obstruction. Clinicians have been led to consider coronary thrombosis as nearly always a very acute incident. The explanation that Dr. Leary gives, the rupture of an atheromatous abscess, helps to explain why many cases are acute. But clinicians—perhaps the pathologists can explain why—certainly see some cases that they call acute where not for minutes, but for many hours, there are prodromal symptoms preceding the major outbreak. If an atheromatous abscess ruptures into the coronary, as I understand Dr. Leary, this really makes a plug at the point of narrowing. Is that always associated with an acute clinical manifestation? Are there cases in which the débris spills out into the lumen more gradually? Is this débris at times so thin, so fine, that it may be distributed distally, causing thus, as it lodges in the finer twigs, a disseminated thrombosis with patchy fibrosis as an ultimate result?

Dr. Leary referred to a fact about which I was going to speak, that there are cases in which a break in the wall of the vessel is followed by the entrance of blood into the wall of the vessel, really a dissecting aneurysm. My attention was first called to this occurrence by Dr. Gideon Wells of Chicago who said that he had noticed it in several cases. Dr. Moody of San Francisco showed me specimens that illustrated it. I recall also that Hyman and Parsonnet described a case. Is such dissecting aneurysm frequent?

This work is of such fundamental importance and has so many possible far-reaching bearings that it should be continued by Dr. Leary and confirmed by other investigators before being accepted in all its details.

Dr. Emanuel Libman, New York, N. Y.—I am not at all sure that rupture of atheromatous pockets will always lead to thrombosis, because one may encounter very extensive superficial areas of atheroma without any thrombosis supervening. I have drawn attention to the probability that there is an individual tendency to thrombosis (thrombophilia), and Dr. Herrick has just referred to the same subject. Thrombosis may occur in a vessel that is not much altered. On the other hand, extensive atheroma may occur throughout the aorta, without a trace of thrombosis. In another case of the same kind, there may be a thrombotic deposit in practically all the lesions. We know that atheromatous material may be discharged into the circulation, and occasionally one comes upon embolic lesions (skin) due to it.

While I believe that spasm occurs in the coronary arteries, it is difficult to secure post-mortem proof. It is possible that with careful studies, evidence may be obtained. I say this from an analogous finding. Many years ago, in a case of lead intoxication—fatal, due to intestinal obstruction—I found the last 18 inches of the ileum tightly contracted, although the examination was not made until several hours after death.

I would like to come back to Dr. Leary's main thesis, namely, the diathetic and metabolic aspects of coronary artery disease. For example, there is in some individuals a tendency to lay down connective tissue. This subject will now be more widely discussed because of the recent remarkable studies of Doljanski. In the course of studies in tissue culture, he was able to develop fibrillar tissue in plasma, with the aid of cellular products and in the absence of the cells themselves.

Furthermore, there is an individual tendency toward calcification. With regard to the subject of cholesterolemia and cholesterol deposition, I believe that a hepatic disturbance is primary. For some time I have held the opinion that in the con-

ditions which are commonly called "gouty" the disorder is largely connected with a disturbance in lipoid metabolism.

I should like finally to say a word in connection with the increasing frequency of coronary thrombosis. I believe that you will all agree that we now see fewer people in the street than formerly, who show the results of a cerebral thrombosis. It is possible that a number of those who formerly died of cerebral thrombosis at a late age, now die of coronary thrombosis earlier in life.

Dr. R. W. Scott, Cleveland, Ohio.—I should like to bring up for consideration here the younger group of patients that Dr. Leary mentioned whose coronary disease was characterized by fibrosis. I have been interested in such cases because of the obscure picture from an etiological standpoint which they present clinically. The ordinary signs and symptoms which aid us in establishing an etiological diagnosis are often absent. The patient runs a progressive downhill course, often extending over a period of several months. Advanced congestive failure is usually present at the time of death, and, as a rule, the diagnosis of coronary disease and myocardial fibrosis can be made only by exclusion.

I wonder whether Dr. Leary has any ideas as to the capricious distribution of the arteriosclerotic process in the aorta and the coronary arteries. Why is it, for example, that individuals who live seventy years or more have at autopsy no disease in the first two inches of the aorta? Why is it that the arteriosclerotic process may be sharply localized in a small area of the coronary artery and the remainder of the vessel show little or no involvement?

Dr. Edward B. Krumbhaar, Philadelphia, Pa.—While of course agreeing with Dr. Herrick as to the interest and stimulus attached to this point of view and to the evidence presented, I want to insert a word of caution, which doubtless Dr. Leary would agree with, that we should not on this account remove milk and eggs from the dietary! In the first place, results of metabolic studies on herbivorous animals such as rabbits must be transferred to man with great caution. Also there would have to be a correlation demonstrated between a high cholesterol intake and these lesions or at least some objective evidence of disordered cholesterol metabolism.

Dr. Walter W. Hamburger, Chicago, Ill.—I should like to ask Dr. Leary whether at autopsy he found similar changes in other vessels throughout the body. For example, in the renal artery or in vessels of the stomach and the spleen, whether changes in young and old individuals occurred in these vessels similar to changes in the coronaries.

Dr. J. P. Anderson, Cleveland, Ohio.—I should like to ask one question about the lipoid cells—Do they represent a fixed or wandering type of cell, i.e., are they endothelial cells engorged with lipoid material, or do they represent a fixed connective tissue type of cell in the arterial wall that imbibes the lipoid?

Dr. Harold E. B. Pardee, New York, N. Y.—I wish to ask Dr. Leary whether it is not difficult to distinguish between the grooving of the wall which he believes due to spasm, and such grooving as might result if the inner layers of the arterial wall were swollen and increased in volume, so that the circumference of the inner layers would be greater than the circumference of the outer layers.

Dr. Timothy Leary.—With reference to the frequency of acute thrombotic processes in coronary arteries it should be kept in mind that the material I have to deal with is derived from sudden deaths, occurring usually with little or no warning, and without medical attendance. My statistics show a definite increase in the numbers of this type of case. I am satisfied that the hard winter we went through had an influence in bringing to a termination many cases of coronary disease. I have certified

as many as six deaths of coronary type in one day this spring. The only symptom in most cases had been indigestion, which is more significant than angina in relation to sudden death. The character of the lesions found leaves no doubt as to the acuteness of the thrombosis. Coronary infarction is exceptional in this series.

Dissecting aneurysms of the coronary are rare in the literature and in my experience.

We recognize that the contents of an atheromatous abscess of the aorta are usually diffused without symptoms as far as they are recognizable. The delivery of a mass of semisolid mushlike material into a narrowed coronary artery, in my experience, tends to clog the artery locally, and is the standard cause of death in older persons. That this obstruction of the lumen by the contents of an atheromatous "abscess" is not an artefact is indicated by the occurrence of thrombi mixed with the contents of the atheromatous pocket in a high percentage of the cases. It is difficult to diffuse these contents through fluid blood, since they do not mix readily. It is impossible to diffuse the contents through clotted blood by any procedure which might be carried out post mortem. The influence of spasm in forcing the contents out of the atheromatous "abscesses" is suggested by the finding of the contents in the lumen and the cavity from which they came relatively empty and containing little blood. Rupture in the other direction, from the lumen into the "abscess," is found occasionally. The formation of clots on the site of ruptured atheromatous pockets in the aorta depends upon the area denuded of endothelium. If the "abscess" has ruptured through a small opening, no clot is formed. If the rupture includes wide tearing of the intima, thrombosis occurs.

This work should not lead to too critical an attitude toward eggs and milk. Cholesterol is a necessary part of the diet, and is important particularly in the growing period. The problem is basically one of metabolism. All the cholesterol in all the arteries in a patient with advanced atherosclerosis would weigh ounces at most. When one considers the years required to produce this deposit, the daily increment must be small. Perhaps we shall be able later to find some indicator on which we can base an estimation of the ability of the individual to handle cholesterol. Measures of the mobilized blood cholesterol will not suffice.

In none of my cases was there indication of myocardial insufficiency preceding the death, other than indigestion or a tired feeling. In only one of the cases was there evidence of so-called chronic myocarditis.

The connective tissue lining the coronary which is thrown into folds is not swollen. It is redundant and has a certain rigidity, but the fact that it is thrown into folds is evidence of narrowing of the lumen of the vessel, due to muscular tonus or to contraction.

We have no evidence as yet to offer with reference to the degree of atherosclerosis in other vessels.

It is my belief that the lipoid cells arise from the subendothelial connective tissue, though others believe them to be monocytes from the blood.

The work here discussed is presented not as a completed study, but as a report of progress. The Committee on Scientific Research of the American Medical Association has extended to me a further grant in aid for prosecution of added work. I shall be grateful for criticism in any or all phases of the subject.

Discussion of paper on "Coronary Arteriosclerosis, Coronary Thrombosis and the Resulting Myocardial Changes" by Drs. Saphir, Priest, Hamburger and Katz.

Dr. Edward Krumbhaar, Philadelphia, Pa.—I should like to speak of some relevant studies made by Dr. Polanco in our pathological department, where the amount of coronary sclerosis was observed in the various branches and correlated with the item of cardiac pain. Two hundred and thirty-six cases were analyzed in which

coronary disease was sufficient to be mentioned in the anatomical diagnosis. Sixty per cent of these, in our opinion, were really marked coronary sclerosis, and yet there were only thirty-four that showed any evidence of cardiac pain, and only ten showed old or recent coronary occlusion. Of these ten, only six had a history of cardiac pain. We did think, however, that we saw just what Dr. Saphir has emphasized, namely, that where there was coronary occlusion, sometimes it was multiple and sometimes the size of the infarct was undoubtedly influenced by a neighboring marked sclerosis, if not total occlusion.

We also studied sections from forty-four patients in six different parts of the heart and also in different organs of the body. We found that in all tissues examined there was some sclerosis, but the amount of sclerosis differed greatly. The heart, kidney, and spleen showed the most of any organs; in the others, it was almost negligible from the functional point of view. The same sort of thing was found in the six different parts of the heart. The descending branch of the left coronary was much more sclerosed than the others. Strange to say, the posterior descending was much less sclerosed than either of the circumflexes and was sclerosed to about the same degree as the two marginal arteries. Such findings merely emphasize again the patchy nature of the arteriosclerotic process and the need, if one is going to make an adequate study, of a very careful examination of all parts of the heart and the coronary distribution.

Dr. Emanuel Libman, New York, N. Y.—It is very interesting that Dr. Saphir and his colleagues found that in all their cases of infarction, two vessels were closed. I should like to know whether they feel that it is essential for infarction that branches of both the left and the right coronary arteries be blocked. According to my experience, this does hold true for infarction of the left posterior papillary muscle. This structure is supplied by the descending branches of both coronary arteries, and infarction occurs only when both are involved.

As regards the instances of infarction without closure of any large branch, the explanation lies partly in cumulative closure of small vessels. Apart from this, one must consider the question of spasm, and the possibility of toxic edema and toxic necrosis. Some years ago I observed a patient, suffering from subacute intestinal obstruction due to a carcinoma of the cecum, who developed a loud systolic murmur to the left of the sternum, which proved to be due to a perforation of the septum, secondary to necrosis. The heart showed a number of areas of necrosis, without any disease of the vessels to explain them.

Related to the studies of Dr. Saphir and his associates are some observations that I have made relating to the occurrence of jaundice in cases of coronary artery thrombosis, when not dependent upon another cause. In the cases that I have seen, few in number, there was present an old closure on the right side, and a recent one on the left. The explanation that has occurred to me is as follows: The closure on the right side leads to a disturbance of liver function. When occlusion of a large vessel on the left side then takes place, the collateral supporting the right side of the heart is much cut down, and there results a sudden increase in hepatic insufficiency. In organic disease of the tricuspid valve, jaundice not uncommonly supervenes, but it takes a long time—many years—for it to come. In these coronary cases it comes quickly, and therefore a remarkable opportunity is afforded for a study of acute hepatic insufficiency. I should like to know whether Dr. Saphir and his coworkers have had any experience with this subject.

Dr. Hamburger reported a number of years ago a case of jaundice associated with coronary thrombosis. I do not know whether a post-mortem examination was performed.

[Dr. Hamburger answered—No.]

Dr. Otto Saphir.—Dr. Priest a little later will discuss the relation of coronary thrombosis to pain as found in our thirty-four patients. I may say now that there was no relation at all between coronary thrombosis, severe coronary sclerosis and myocardial changes on the one hand to pain on the other hand.

In none of the hearts was there an infarct as the result of the occlusion of one branch of the coronary artery. Necrosis or infarction of the posterior papillary muscle was not encountered in this series.

The sclerotic process often extended into the smaller branches of the coronary artery. The arterioles, however, in none of these instances were diseased. As far as our experience goes, I might state that arteriolosclerosis of the coronary artery is rare.

None of the patients with coronary thrombosis revealed jaundice.

Discussion of paper on "A Clinical and Pathological Study of Coronary Sclerosis" by Drs. Elliott, Evans, and Nuzum.

Dr. Robert L. Levy, New York, N. Y.—Dr. Nuzum said that there were certain cases which showed *practically* no coronary sclerosis. It is very difficult to determine, on a quantitative basis, just what degree of coronary sclerosis is functionally significant. Sometimes, what appear to be minimal lesions may be of great clinical importance. In the presentation which will be given later in the day by Dr. Turner, Dr. Bruenn, and myself, this fact will be stressed particularly in relation to pain.

Discussion of paper on "The Relation of Coronary Arteriosclerosis to Auricular Fibrillation With Special Reference to the Term 'Arteriosclerotic Heart Disease'" by Drs. Brown and Levine.

Dr. Wellace M. Yater, Washington, D. C.—I was surprised to see that this was the only paper on the program which had to deal with the arrhythmias relative to coronary sclerosis. Some years ago I made a study similar to this very interesting one of Drs. Brown and Levine on the pathological changes in cases of auricular fibrillation. Of 145 patients who came to necropsy there were only two hearts which had any great degree of coronary sclerosis, and both of these patients had shown hypertension clinically during life. I was forced to the conclusion that coronary sclerosis per se was a very rare cause of auricular fibrillation. There are, however, some arrhythmias, or better conduction disturbances which are definitely due, quite frequently, I believe, to coronary sclerosis. I refer particularly to auriculoventricular heart-block and bundle-branch block.

In a study of the conduction system by serial sections in cases of this kind. Cornell and I were struck by three things which I believe are relatively new: first, that A-V heart-block is not infrequently due to isolated lesions of the bundle branches, secondary to coronary sclerosis either of the large arteries or of the small ones; second, that it is extremely rare to find that only one bundle branch is involved by fibrotic changes and not the other; third, that the bundle branches may be extensively involved without any apparent pathological changes in the myocardium. It would seem, therefore, that the conduction system is more susceptible to a diminution of vascularity than the myocardium and shows changes sooner. We were unable to confirm the newer classification of bundle-branch block because of the great paucity of cases which have lesions confined to one bundle branch. This fact has been noted also by other workers.

I think the time has come when we need more studies by means of serial sections through the conduction system, because I believe we are drawing too many anatomical conclusions from electrocardiographic studies.

Dr. Louis F. Bishop, New York, N. Y.—I have been much interested in Dr. Levine's paper because we have made a recent study of so-called arteriosclerotic auricular fibrillation from the clinical standpoint. Dr. Levine stated that 80 per cent of the patients who came to necropsy had had hypertension. We found in our study somewhere around 50 per cent had hypertension, but a large number of these were women.

Dr. John J. Finigan, Rochester, N. Y.—I should like to ask Dr. Levine just one question. Just what age group did these fifteen patients with fibrillation fall into? Did they belong to the older age groups of sixty and seventy years, or to the younger age groups?

Dr. Samuel A. Levine.—Naturally we did not analyze the incidence of other types of arrhythmia, being concerned entirely with auricular fibrillation.

I think Dr. Yater's point is an important one. Fibrillation in coronary artery disease is not common. The arrhythmias he speaks of are common in acute coronary thrombosis. There is a great difference between proper and improper treatment of complete heart-block in acute coronary thrombosis. It may mean the difference between life and death. It is one of the few complications, I believe, in which the physician can function in a very important sense.

Dr. Bishop spoke about an incidence of 50 per cent of hypertension in his cases. I think our figure is a little greater because we included among those having hypertension those who had normal pressures at the time, but who were known to have had previous hypertension or well-marked changes in the retinal arteries, indicating a previous hypertension. The females are more hypertensive than the males in all cardiovascular diseases, and particularly in coronary artery disease—decidedly so.

We did not even think about the relation of possible chest injury to these cases. Dr. Finegan asked about the age groupings. I do not recall them accurately. We have them in our paper. I regret we did not regard it as important enough to indicate the exact ages. The fifteen patients with auricular fibrillation without heart disease included the five thyroid patients that we overlooked years ago (as I recall them, they were middle-aged people), six others with infections such as pneumonia, and four who had nothing to account for the fibrillation, who died of entirely unrelated conditions like leucemia or brain tumor.

Discussion of papers on "The Relation of Arteriosclerosis to Hypertrophy of the Heart" by Dr. Carr; and "Arteriosclerotic Heart Disease: Coronary Thrombosis and Its Effect on the Size of the Heart" by Drs. Horine and Weiss.

Dr. Ernst P. Boas, New York, N. Y.—I think it is the experience of most of us that in accordance with Dr. Weiss's study, a simple coronary occlusion is rarely ever followed by cardiac enlargement. I am under the impression, however, that, although a single coronary closure followed by survival for a number of years without heart failure is not followed by cardiac enlargement, in those patients who have multiple episodes of coronary closure, or who have slowly progressive subclinical closures with multiple myocardial infarcts, cardiac enlargement does occur.

I can recall two patients whom I have observed for a good many years, who had never had hypertension, and in whom cardiac enlargement occurred in the course of several years following multiple coronary episodes. It is my impression that the cardiac hypertrophy which always follows signs of cardiac insufficiency is in some way related to failure of the heart muscle.

Dr. Samuel A. Levine, Boston, Mass.—I should like to ask Dr. Weiss whether he has any information on the size of the heart temporarily. Is there some temporary dilatation?

Dr. W. R. Williams, Riverside, Ill.—I should like to ask Dr. Carr two questions. Does he find that adequate coronary circulation is essential for the development of the hypertrophy? In sclerosis of the coronary arteries, is this a late development in an already hypertrophied muscle?

Dr. James G. Carr.—The idea brought out in Dr. Williams' question occurred to us, but we have found no support for the view that a normal coronary circuit is more likely to be associated with cardiac hypertrophy than one with marked arteriosclerosis. It does appear that marked coronary sclerosis is frequent in connection with large hearts, especially in association with hypertension.

The most significant result of this study is the demonstration of many large hearts for which no cause can be assigned. Granting that the hypertrophy in many instances may have resulted from hypertension which had receded before the final illness, we are not justified in thus dismissing the entire group. In the presence of the data here presented, one may not deny the possibility that we are habitually overlooking causes of cardiac hypertrophy not now included in our categories.

In conclusion, attention should be directed to a few cases of a different type which are equally difficult to explain, namely, a few hearts weighing less than 325 grams which were associated with systolic blood pressures of 200 and above.

Dr. Morris M. Weiss.—We did not note at any time temporary dilatation of the heart immediately following the acute occlusion.

Those who state that coronary occlusion can cause cardiac enlargement do not mention the size of the heart at the time of the acute obstruction.

Clinical and pathological evidence of a preexistent hypertension should always be sought in any patient with an unexplained cardiac enlargement. As a result of coronary thrombosis a blood pressure previously high may fall to normal clinical limits and remain so for the remainder of the patient's life.

Our report did not discuss theoretical functional pathology. Some claim that from a functional point of view slow obliteration of coronary vessels must lead to cardiac enlargement. From analogy to vascular disease in other organs, coronary disease should theoretically result in atrophy of the heart.

Discussion of paper on "Arteriosclerotic Heart Disease in Diabetes" by Drs. Root and Sharkey.

Dr. Louis N. Katz, Chicago, Ill.—In some work carried out in collaboration with Drs. Soskin and Sol Strouse, we pointed out that when diabetes and heart disease are associated, the cardiac condition cannot be neglected in the therapeutic procedure for the diabetes. It was found unwise, in many such cases, to treat the diabetes too rigidly since the improvement in the diabetic manifestations was accompanied by a subjective and objective deterioration in the cardiovascular status. These patients reacted very favorably to a high carbohydrate diet, and it appeared that the blood sugar level consistent with well-being in such patients is higher than that which is considered desirable in diabetic patients without cardiovascular disease.

Dr. Samuel A. Levine, Boston, Mass.—There is a very important point involved in this topic in the relation between angina pectoris and diabetes. If diabetes is the causative factor and has something to do with the development of angina, treating diabetes rigidly will be a preventive in the life history of angina patients. I do not believe that this relationship has yet been proved.

It would seem to me that if diabetes were productive of angina pectoris in a causative sense, the patient who has diabetes ought to have angina earlier in life and die earlier in life than nondiabetic angina patients. Years ago the analysis we made of the nondiabetic and the diabetic patients with coronary thrombosis showed that they got the disease and died at about the same age. Dr. Root's figures today—63

years for hypertensive and 51 for nonhypertensive—are approximately the age of death from coronary artery disease in nondiabetic individuals. Are we not more justified in assuming that both conditions are manifestations of the same inherent defect or tendency? For example, if you took freckled children and nonfreckled children, you would find that more freckled than nonfreckled children have rheumatic heart disease. That is to say, the freckles may indicate a vulnerability to the disease. If we took two diabetic twins coming from parents with diabetes or vascular disease, one kept from developing diabetes by treatment and by prohibiting obesity, might it not be that we would find both to have coronary artery disease at the age of forty-eight or fifty-three years, the one a well-treated diabetic who had been prevented from becoming obese, the other definitely obese? Our figures on angina and obesity show the same thing; that obesity does not enhance the development of angina. May not obesity and diabetes be mere homologs indicating the same type of vulnerability?

Dr. Wallace M. Yater, Washington, D. C.—In the same connection as Dr. Levine's discussion, I wonder whether Dr. Root noticed a greater incidence of coronary sclerosis among the treated diabetic patients than among the untreated.

Dr. H. F. Root.—It is difficult to classify patients according to the degree of successful treatment and control of diabetes. A perfectly treated diabetic person is rare. Furthermore our standards of proper treatment have changed rapidly in the last fifteen years. We think some of our patients are well treated, but we do not know what happens to them a large part of the time. Everybody knows that diabetes in patients may be severe this year and next year may be mild; the year after that be severe again. The duration of the disease is one thing that you can be pretty definite about, and whether the patients are young or old, the duration is an important thing.

Modern treatment is better than the old treatment. I am sure more judicious use of insulin gives better results than in the past, and we are seeing fewer calcified arteries in the legs of children. Autopsy findings shed some light on the question of whether the vascular lesions are due to an inherited tendency or are secondary to the diabetes. Shields Warren examined a series of nearly 300 nondiabetic persons, and found as much arteriosclerosis in the pancreatic vessels as in the diabetic persons. Second, he examined nearly 300 diabetic individuals and found only 27 per cent had arteriosclerosis in the pancreatic vessels.

Dr. M. H. Nathanson, Minneapolis, Minn.—Several years ago I made a similar study on one hundred autopsied diabetic persons. I compared the incidence of coronary disease with a group of 250 nondiabetic persons. Fifty-two per cent of the diabetic patients above the age of fifty years showed extensive coronary disease as compared with an incidence in the same decades of 8 per cent for the nondiabetic group. Thus, the incidence of extensive coronary disease was six and one-half times greater in diabetic than in nondiabetic persons.

In the nondiabetic individuals the preponderance of males over females showing coronary disease was 3 to 1. In the diabetic series the ratio was 1.8 to 1. This indicates that the comparative immunity of the female to coronary disease is distinctly lessened when diabetes is present.

The mode of death was also studied. About one-half of the diabetic patients showing severe coronary disease died a cardiac death. Of these two-thirds died of congestive heart failure and in one-third the death was anginal in type.

The age incidence of diabetes is important. We know that 10 per cent of all the cases begin in childhood without arteriosclerosis. Forty per cent of them begin before the age of forty years. Diabetes disappears in old age. We now know that the peak of incidence in diabetic persons is between fifty and fifty-five years and per-

haps earlier. Then incidence falls, and at seventy a man is no more likely to develop diabetes than he was at twenty. This significant observation of Pincus and White is rather against the supposition that arteriosclerosis causes diabetes.

I am very grateful for the comments of Dr. Nathanson. The great frequency of coronary disease seems to me incontrovertible and the emphasis should be upon judicious treatment. The fact that extremes of chemical change in blood and tissues either in one direction or the other in the diabetic have a bad effect upon coronary disease, seems indicative of a metabolic influence.

Discussion of paper on "Valvular Atherosclerosis" by Drs. McGinn and White.

Dr. Emanuel Libman, New York, N. Y.—This important subject is now receiving some of the attention which it deserves. For a long time the calcific lesions of the heart, whether secondary to an inflammatory process (rheumatic fever, subacute bacterial endocarditis, etc.), or not, have been neglected. Because the term "Mönckeberg's sclerosis" is so much identified with the Mönckeberg calcification of the media of arteries, I believe it would be advantageous to designate the valvular lesion discussed by Drs. McGinn and White, "Mönckeberg valvular lesion," or still better, "annular fibrosis or sclerosis," and if calcification be present, "annular calcification" or "ring calcification."

There is a murmur which is often characteristic of calcification of the mitral ring, and by means of which one can at times suspect its presence, in persons over thirty-five to forty years of age. It is a systolic murmur heard best to the left of the sternum. It may be present along the left sternal margin up to the position of the pulmonary artery. The first sound is generally audible, merging directly into the systolic murmur which is likely to be rough, often whistling in character, at times musical. It is transmitted to the right as much as to the left, and is less loud at the apex. It is usually not heard beyond the apex. If there be present a similar murmur in the area of the aortic orifice, one must be cautious in venturing an opinion because the parasternal murmur may be only a transmitted one.

This subject is very important, because in rheumatic fever there is often heard a murmur in the same position, especially early in the disease. It is likely to be somewhat rough in character, not smooth like the early murmur of insufficiency, which is loudest at the apex and markedly transmitted to the left. Because of my experience with the murmur due to ring calcification (and ring sclerosis ?) I have for a long time suspected that the murmur heard best in the same location in rheumatic fever may be due to valvulitis of the mitral ring (perhaps at times, valvulitis of the pulmonary artery). This murmur not infrequently disappears when a mitral insufficiency develops, resulting from sclerotic changes at the free border of the valve. In cases of rheumatic fever it is important to listen carefully at the left border of the sternum, as well as at the apex and base of the heart.

Sibson knew of this early murmur in rheumatic heart disease, and described it with great care. He interpreted it as being due to relative tricuspid insufficiency. This explanation cannot be correct, because if it were, the murmur should become louder when a real mitral insufficiency develops. Like some other observers, however, Sibson himself noted that the murmur often disappears as a mitral insufficiency develops.

Dr. McGinn.—It is true, we generally think of Mönckeberg's sclerosis as medial sclerosis of the medium-sized peripheral arteries. Mönckeberg has also described a distinct atheromatous and sclerotic change involving the base of the aortic cusps and in this same paper has given a remarkably clear description of the histology of the aortic valve cusps. To retain the name of Mönckeberg's sclerosis of the aortic valve for these lesions would direct attention to his valuable observations. A similar process

may, however, involve the mitral valve so that the term "annular sclerosis" may well include such lesions of the aortic and the mitral valve under one terminology and is probably preferable to Mönckeberg's sclerosis.

Discussion of paper on "Coronary Arteriosclerosis, Coronary Thrombosis, and the Resulting Myocardial Changes" by Drs. Priest, Hamburger, Katz, and Saphir.

Dr. Morris M. Weiss, Louisville, Ky.—Some racial and social observations on pain in coronary artery disease may be of interest. A history of classical angina pectoris is uncommon in the Louisville City Hospital patients with coronary disease, whereas it is a frequent complaint in our private cases. It is especially rare in negroes, although they have coronary disease with a frequency equal to that in the white race. We believe this is due to the lack of intelligence of the average city hospital patient, especially the negro, who is unable properly to interpret and describe his symptoms.

Pain lasting a half hour or more or a marked fall in blood pressure are considered pathognomonic of a coronary occlusion. This has not always been our experience. Attacks of angina pectoris may last up to two hours without subsequent clinical evidence of coronary thrombosis. Also the blood pressure may temporarily rise during a coronary occlusion.

Dr. Walter S. Priest.—I am glad Dr. Weiss emphasized the points that he did. From the results of this study, I know some of us have become reluctant to make a positive diagnosis of coronary thrombosis or myocardial infarction in any given case.

Dr. Weiss emphasized the pain feature and the blood pressure feature. Again referring to the patient whose slide I showed; when one can see a patient have an attack of pain lasting as long as four hours and associated with the other characteristic clinical symptoms and yet not have a coronary thrombosis or myocardial infarction, it makes one wonder whether many of these attacks which we have diagnosed clinically as undoubted coronary thrombosis should have been so diagnosed.

Discussion of papers on "Significance of the Coronary Circulation in Arteriosclerotic Heart Disease" by Drs. Smith, Paul, and Rathe; and "Mechanism of Pain Production in Angina Pectoris" by Dr. Katz.

Dr. Joseph B. Wolffe, Philadelphia, Pa.—The paper presented by Dr. Katz and the one by Dr. Smith are extremely important from a clinical point of view. They tried to show that one must keep in mind other factors, not only coronary disease as the causative factor in precipitating the painful syndrome of angina pectoris.

Dr. Katz presented experimental evidence to support the theory that angina pectoris may be of neurogenic origin. It has been shown that many nociceptors like an abnormally functioning thyroid, gallbladder, psychic and metabolic disturbance may be responsible for the syndrome of angina pectoris.

I have already called attention to the possibility not only that angina pectoris is frequently of neurogenic origin, but that coronary T-waves may be caused by neurogenic disturbances. I have shown that pancreatic extract apparently due to its lecithinogenic property and its influence upon muscle metabolites, tends to relieve angina pectoris and intermittent claudication.

This points to the possibility that metabolic, particularly lecithinogenic, dysfunction, may be another factor in the causation of angina pectoris. Dr. Smith stresses coronary disease as an etiological factor in angina pectoris, and Dr. Katz calls attention to the possible neurogenic elements in angina pectoris. We therefore should still keep an open mind as to the many possible causes of this symptom complex.

Dr. Walter W. Hamburger, Chicago, Ill.—I should like to ask Dr. Smith this question: Was the paroxysmal dyspnea usually nocturnal in origin, and if so does not Dr. Smith feel that paroxysmal dyspnea is usually a sign of left heart failure, as Paul White and others have declared? And if he does feel that paroxysmal dyspnea is a sign of left heart failure, does he believe that such attacks always mean occlusive changes in the coronaries, particularly in the left side of the heart?

Dr. Walter S. Priest, Chicago, Ill.—In connection with Dr. Smith's mention of the development of angina of effort following coronary occlusion, I might state that in the group I reported this morning 30 per cent of the patients who had angina of effort developed the angina of effort following coronary occlusion or myocardial infarction.

Dr. Andrews.—Some time ago I had the opportunity to observe a patient who had a phlebitis migrans in which at one time or another most of the vessels throughout the body were thrombosed. At one period in her course, she had some precordial distress, and the electrocardiogram became abnormal. It was my impression at that time that she had thrombosis of some of the coronary veins. The significance of it did not impress me at that time, but I have wondered many times since whether that did not involve a disturbance in the carrying away of the various waste products and gave close to an anginal syndrome.

Dr. Katz's observation here in regard to the compression of the coronary arteries and veins has been very interesting to me.

Dr. Harold E. B. Pardee, New York, N. Y.—I, too, have seen a case very similar to the one just mentioned in which phlebitis migrans was followed by a typical clinical picture of coronary occlusion with electrocardiographic changes. It seems quite evident that this picture may result from venous as well as from arterial disease.

I wish also to emphasize one of the things which appeared in Dr. Smith's paper, that is, the great frequency of the syndrome of cardiac insufficiency. The development of this syndrome is a well-recognized result of coronary arteriosclerosis, but it happens that the present fashion of diagnosis and treatment has led us to talk very much more about the anginal syndrome. I noticed that in Dr. Smith's series the cardiac insufficiency syndrome was the most frequent clinical picture.

Dr. Oille, Toronto, Ont.—We also had a patient with phlebitis migrans who developed symptoms and electrocardiographic findings of coronary occlusion. Thrombosis in the coronary sinus was diagnosed and proved at autopsy.

I should like to emphasize Dr. Pardee's last remark and stress the point that dyspnea is a common and perhaps a more important manifestation of coronary disease than pain. Dr. Rykert and I have recently analyzed the last ninety cases of severe coronary disease that came to autopsy in the Toronto General Hospital. Of these, the largest group was characterized by dyspnea and congestive failure. In addition, dyspnea appeared to be a more serious symptom than angina, because, in the patients whose first symptom was angina, the duration of life averaged forty months. In those patients whose first symptom was dyspnea, the average length of life was twenty-eight months. The duration of life after nocturnal dyspnea commenced was eleven months. These figures, of course, are not averages for all cases of coronary disease, but merely represent the average length of life of this serious group of ninety individuals.

Dr. Laplace, Philadelphia, Pa.—I should like to call attention to a further analogy between angina pectoris and experimental muscular ischemia as described by Dr. Katz. Dr. Martin Crane and I have performed similar experiments on a

series of hospital patients and found that many subjects developed muscular fatigue which terminated the exercise before the appearance of severe pain. We concluded that an explanation of the absence of pain in many cases of myocardial ischemia might be found in the possibility that in such cases fatigue may prevent the cardiac muscle from working to the point of pain production. Our experiments were originally designed as a quantitative test for sensitivity to the pain of muscular ischemia. We found that no abnormal sensitivity of this type could be demonstrated in patients with angina pectoris, and we concluded that nervous hypersensitivity is therefore unlikely to be an important factor in determining the occurrence or degree of pain resulting from myocardial ischemia.

Dr. Fred M. Smith, Iowa City, Iowa.—Paroxysmal dyspnea is commonly indicative of a left ventricular failure. We wished to emphasize the importance of bearing in mind the possibility of coronary occlusion, especially with the first attack and particularly in those who heretofore have been free from cardiac symptoms. The paroxysmal dyspnea frequently occurs at night, but in several instances of our series first appeared during the day following exertion.

We were impressed with the high incidence of congestive failure as the initial manifestation of cardiac disease in our series of cases. It was felt that in certain instances the congestive failure followed an unrecognized coronary occlusion. The prognosis was in general graver in this group of patients. There was little time to speak of electrocardiographic findings, but you may be interested in knowing that 30 per cent of those beginning with congestive failure had bundle-branch block. The incidence of this finding was highest in this particular group.

Dr. Louis N. Katz, Chicago.—We found two factors primarily concerned with the production of pain. The first is ischemia, and the second is the state of the nerve apparatus. Our work has led us to conclude that ischemia produces a chemical substance, diffusible in character and probably acid in nature, which acts as a stimulus for pain production. Our work has shown that the pain produced by occlusion of the coronary vessels in the dog is due to irritation of the sensory nerve fibers and not to occlusion of the artery itself.

Our experiments further show that these pain fibers are confined to the region of the coronary vessels. Pain responses were not obtained when other regions of the myocardium were compressed. Woollard has shown that these sensory fibers congregate around the mouths of the coronary vessels. It is conceivable that the involvement of these fibers by syphilis at the root of the aorta might explain the anginal attack, without invoking actual occlusion of the mouths of the coronary vessels. Similarly the blind manipulation involved in probing the mouths of the coronary arteries, such as carried out by Sutton and Lueth, might easily give rise to pain by stimulation of the nerve plexus surrounding the coronary mouths and not, as they assume, by closing off the coronary blood supply. Even sudden death preceded by agonal struggle might be due to ventricular fibrillation, the direct or reflex result of stimulation of this plexus.

We have obtained evidence that fatigue is a variable which modifies the pain response from skeletal muscle. We have found in our work that fatigue is a disturbing element. The subject, as first pointed out by Laplace, may, on occasion, stop contraction because of fatigue and not unbearable pain. In one subject we found that, following a short period of bodily exercise, the subject was unable to contract the muscles after his arm was made ischemic because of fatigue. It may be that the element of fatigue determines whether signs of congestive failure or anginal attacks occur in coronary sclerosis. This concept, however, demands further proof.

Discussion of Symposium on Electrocardiogram Phases of Coronary Arteriosclerosis.

Dr. Louis N. Katz, Chicago, Ill.—There are a number of things that might be discussed but the limitation of time will permit me to take up only one or two. The concept presented by Hiss and Robb that the contour of the electrocardiographic distortion is determined by the bundle of muscle involved is very interesting and may be the ultimate solution of our inability to locate infarcts accurately with ordinary leads. The result of work done in our laboratory indicates that the electrical currents are conducted away primarily by the posterior muscle mass. It might well be that the conduction of electric currents may be best along the muscle bundles, and so the electrocardiogram will depend on the location of the muscle bundles to the posterior muscle mass.

The plea of Dr. Barnes to utilize the ordinary leads more than we are before introducing any other leads cannot pass unchallenged. I think there is today a temptation to read into the standard leads significance based on very minor changes which might easily be subject to personal interpretation. This tendency makes the reading of electrocardiograms a mysterious process to the average physician. From a personal experience with an extensive series of electrocardiograms I am convinced that the electrocardiogram is very valuable in the interpretation of coronary disease. The use of chest leads has been a valuable addition. While I do not advocate the use of nine leads for ordinary purposes, I feel, from the experience of Wilson, of Wolferth and Wood and at our Heart Station, that many cases of recent coronary occlusion would be missed if a fourth (chest) lead were not taken. We feel that the position of the anterior electrode is important: the posterior one can be placed practically at will. While the ordinary three leads have not been very useful in our hands in locating infarcts, the fourth lead has so far been infallible in our autopsy cases. It would be a pity to discourage the wide use of a fourth (chest) lead, particularly in suspected cases of recent coronary occlusion.

Dr. Samuel Bellet, Philadelphia, Pa.—I should like to mention some of the work we have been doing with precordial leads in conjunction with Drs. Wolferth, Wood and McMillan. At the present time we have a total of 104 cases of coronary occlusion which we have studied by both the indirect and the precordial leads; 22 of these cases have been studied at necropsy. In 40 per cent of these cases, we were able to make a diagnosis by the precordial leads, whereas the indirect lead at one time or another did not clearly indicate such a diagnosis. In addition to the value of the precordial leads in the diagnosis of coronary occlusion, the progression of the lesion can be followed better by the direct chest leads than by any other means at our disposal. This is true chiefly in cases of anterior occlusion. The state of the lesion can be predicted by the configuration of the S-T interval and the T-wave in the precordial leads. These changes may be present for two to three weeks, sometimes for several months, during which time alterations in the T-waves of the indirect leads may or may not be observed.

The precordial leads are also of help in the diagnosis of old anterior infarctions. In the indirect leads the T-waves inverted in Lead I following an anterior occlusion often become upright in the chronic stage. The electrocardiographic diagnosis of such coronary occlusion is impossible from such a tracing as shown in the slide presented by the last speaker. However, examination by precordial leads in the case of anterior occlusion frequently discloses the presence of an old infarction. This is shown by the absence of the initial downward deflection in Lead IV, with no S-T interval deviation. We have had under observation three patients with old coronary occlusions showing the signs just mentioned. In two cases, post-mortem examinations have confirmed the diagnosis; in the other case, the history of a previous

coronary occlusion is quite clear. Many others of our cases followed to the chronic stage, showed similar changes.

The differential diagnosis between the electrocardiographic evidence of acute pericarditis and that of coronary occlusion should ordinarily not be difficult. We have recently had two such cases. The S-T intervals are elevated in all three leads in acute pericarditis, a condition which does not occur in simple coronary occlusion. The differentiation from anterior coronary occlusion is aided by the use of precordial leads which show the maintenance of the initial downward deflection, and the S-T interval situated below the isoelectric line.

Dr. William J. Kerr, San Francisco, Calif.—It seems to me that the paper presented by Dr. Hiss is one of the most important we have heard in some time. I should like to question Dr. Robb concerning the penetrating branches of the coronary vessels. In our experience the penetrating vessels of the ventricles run perpendicular to the superficial branches and supply the muscle clear through to the intima. I should like to ask Dr. Hiss whether his studies suggest that the penetrating branches supply the entire wall. Does occlusion of the vessel at some point near the base cause a selective damage to a certain layer of muscle? If so I cannot understand the function of the penetrating vessels unless they give off collateral branches between layers.

Dr. Jane Sands Robb.—If I may answer a question in regard to these penetrating branches, the superficial muscles obtain their blood supply from certain of the longer branches as they run on the surface of the muscle or between the first and the second layer. There are other branches which are short and give off no superficial branches, but penetrate to the deeper muscles, so that by choosing the branches which one ligates, one can get a lesion in a deep muscle without involving the superficial circulation.

Dr. A. R. Barnes.—I should like to correct an impression that I am against taking direct anteroposterior chest leads. We have taken them on about 2,500 of our patients. I do want to stress the fact that we should not lose sight of the old tools that have served us in good stead and that we should not be carried away by our enthusiasm over the so-called fourth lead.

Dr. Howard B. Sprague.—I agree with Dr. Barnes and Dr. Katz in relation to chest leads. I think that we must use them because of the sort of information that I have reported this afternoon. However, we must decide on the simplest, most efficient method which is clinically practical. There are many reports of electrocardiographic studies using chest and other leads without autopsy control. Autopsy work leads to considerable humiliation, for it is sometimes very disappointing to find that the heart at necropsy does not support the finely spun theories and predictions of cardiac pathology made upon the basis of electrocardiographic study.

Discussion of paper on "Observations on Prognosis in Angina Pectoris" by Drs. Wedd and Smith.

Dr. Samuel A. Levine, Boston, Mass.—I have had similar results as to prognosis in angina pectoris. This last year we published a review similar to the one that Dr. Wedd has given us. We tried to get some clue to predict which patient is going to die in a week and which is going to live for twenty-five years. A few lived only a short time after I saw them, but the extreme was twenty-five years. Blood pressure level did not help; heart size, murmurs, electrocardiograms were a complete disappointment; in fact, we learned something unexpected from them, namely that those who had abnormal electrocardiograms had a longer life, a longer duration of angina, and a greater age at death than did those with normal curves.

There is one point to which I should like to differ, that is the factor of inheritance. We have, I believe, pretty definite evidence in our group that inheritance is important. In fact, the only clue we found is that angina patients who were born of long-lived parents lived longer than those born of short-lived parents.

Incidentally, we have some indirect evidence to show that we inherit the defect from our mothers rather than from our fathers; that is, the female is more responsible for handing down vascular vulnerability, although she suffers from angina a good deal less than does the male.

Discussion of paper on "Treatment of Various Forms of Arteriosclerotic Heart Disease by Means of Total Ablation of the Normal Thyroid Gland" by Drs. Blumgart, Riseman, Davis and Weinstein.

Dr. James Alexander Lyon, Washington, D. C.—I have listened with great interest to the paper by Dr. Blumgart and his associates. The total ablation of the thyroid gland is a major operation and, as has been stated, may be followed by myxedema. Dr. Edmund Horgan of Washington, D. C., and I have obtained very beneficial results in two cases of angina pectoris by performing a much simpler operation; that is, the division and ligation of both superior and both inferior thyroid arteries. As far as we know this operation has not previously been performed in the treatment of heart disease.

In studying a group of 300 patients, five to ten years after thyroidectomy, we made an observation which we considered important. We found that in the cases in the group which had been considered persistent hyperthyroidism, recurrent hyperthyroidism, and "thyrocardiacs," the patients were apparently free of symptoms. There was no evidence of hyperthyroidism, and no tachycardia or auricular fibrillation. These patients had been treated surgically by a method which included the division and ligation of both superior thyroid arteries and the ligation of both inferior thyroid arteries. We concluded from our observation that stopping the effects of hyperthyroidism in these patients was due to two things: first, the removal of the major portion of the thyroid gland; second, and chiefly, the division and ligation of the superior thyroid arteries and the ligation of the inferior thyroid arteries. This latter procedure cut the pathway of nerve stimuli from the sympathetic nervous system to the thyroid gland. As the results of the division and ligation of the superior and inferior thyroid arteries had been so beneficial in the patients referred to above, we considered cutting off the major portion of the blood supply and cutting the nerve pathways from the sympathetic nervous system to the thyroid gland in cases of angina pectoris and congestive heart failure by the division and ligation of both superior and both inferior thyroid arteries. We had an opportunity to perform this operation in two cases; one a patient with angina pectoris who had been observed over a period of five years prior to and five and a half months following operation; and one a patient with aortic regurgitation and angina pectoris who had been observed over a period of seven months prior to and two months following operation. We feel that the clinical improvement in these patients has been so remarkable that the cases should be mentioned here.

The division and ligation of all the vessels at the superior poles of the thyroid gland and the division and ligation of the inferior thyroid artery markedly reduce the blood supply and cut off the sympathetic nerve supply to the thyroid gland. The effect of cutting down the amount of blood entering the thyroid gland and cutting off all stimuli from the sympathetic nervous system is to decrease the basal metabolic rate, to reduce the circulatory demands, and to lessen the work of the heart. We have employed an operation much simpler than the total ablation of the thyroid gland as done by Drs. Blumgart and Berlin. We do not sacrifice a vital organ such as the thyroid or parathyroids. Myxedema is not produced but the basal

metabolic rate is lowered. By leaving the parathyroids undisturbed we do not cause an alteration of the calcium metabolism.

Dr. Samuel A. Levine, Boston, Mass.—We have had about 45 patients operated on by total thyroidectomy at the Brigham Hospital in the past year and a half. The results are similar to those presented by Dr. Riseman. I do not think they warrant quite the same degree of enthusiasm, and yet I have no doubt at all in my mind but that people who were refractory to the methods of treatment we were familiar with have been specifically helped by these procedures.

I think that no one should be operated on who can work without it, or who can be comfortable without the operation; so that very mild cases should not be selected, and those patients who are too sick also should not be selected. There is a group in between where choice can be exercised.

Although this concerns total thyroidectomy, one word might be said about partial thyroidectomy. In the case which made this study of thyroidectomy develop the patient was a woman who was operated on in 1927, who had a partial thyroidectomy done. I followed her for four years, and she had a most unexpected improvement. This was reported about two years ago and precipitated the work subsequently done on complete thyroidectomy.

Dr. Blumgart, after the experience of the first two or three cases we had very properly advised a total removal because a partial removal might be a failure, as the remaining gland could regrow. One of those partial cases, however, is about as good a result as we have had in our entire series. The first patient with partial thyroidectomy of this latter series has been working for about a year and a half. He developed myxedema, in spite of the fact that only a partial thyroidectomy was performed. He had not been able to work at all before, and he is comparatively free from attacks now.

Dr. Herrman L. Blumgart.—The question of subtotal thyroidectomy of the normal gland for the treatment of heart disease is a very interesting one and has been studied by various investigators in the past. Crile, Riesman, Boas and Shapiro, Dautreband, Rose, and others performed subtotal thyroidectomies in patients with no evidence of thyrotoxicosis evidently in the hope that just as this operation lowers the abnormally high rate of thyrotoxicosis to normal, so the normal metabolic rate would be reduced to a subnormal level. While this may occur occasionally, there is no evidence in the literature that subtotal thyroidectomy can be relied upon to produce a permanently subnormal metabolic rate. In the first two cases that engaged our interest, only transient relief was obtained by subtotal removal of the normal gland, the period of relief paralleling the curve of decline in the basal metabolic rate. After some weeks the metabolic rate returned to its preoperative level and the patients' condition relapsed to its previous status. In accord with Halsted's experimental work reported in 1907, we felt that the minute remaining fragments of normal thyroid tissue had undergone sufficient hypertrophy to sustain a normal metabolic rate.

Our earlier work on the circulation, particularly the velocity of blood flow, led us to believe that nothing short of a persistent hypothyroid state with its low metabolic rate would release the heart from its normal burden. Although maximal subtotal thyroidectomy was done in our first two cases, we failed in our primary purpose to reduce permanently the basal metabolic rate. Even if success might occasionally attend subtotal thyroidectomy, it became apparent that nothing but complete removal of every vestige of thyroid tissue would regularly insure a permanent subnormal metabolic rate and clinical improvement.

After success attended the first complete ablation of the thyroid (Case 3 of our first communication, Blumgart, Levine, Berlin: Arch. Int. Med., June, 1933), a

subsequent attempt was made to remove the remaining fragments of tissue in Case 1, in which there had been a relapse to the preoperative clinical condition. Dense adhesions were encountered which made identification of thyroid fragments impossible. It was felt that any surgical dissection would be extremely dangerous because of the difficulty of identification and consequent likelihood of injury to the parathyroid glands or recurrent laryngeal nerves. Heavy dosages of roentgen radiation were employed but without effect.

Our observations (Friedman, H. F., and Blumgart, H. L.: J. A. M. A., Jan. 6, 1934) led to the conclusion that little could be expected from roentgen radiation as a substitute of surgery or an adjunct to subtotal thyroidectomy in the treatment of chronic disabling heart disease. In brief, the failure of others and of ourselves to benefit patients by subtotal thyroidectomy, our unsuccessful attempt to remove residual fragments at a subsequent operation, and the ineffectiveness of roentgen irradiation on the remaining tissue emphasize the therapeutic importance of removing the entire gland at the time of the first operation. Ample confirmation for this conclusion has been obtained by our subsequent experience in some seventy-five cases of angina pectoris or congestive failure, in all of which the hypothyroid state has persisted after total ablation of the thyroid gland, and in practically all the patients clinical improvement has occurred.

At the present time nothing but the complete removal of every vestige of visible thyroid tissue by surgical means will regularly insure the desired persistent hypothyroid state with its lowered metabolic rate and consequent clinical improvement. Recently, since the inception of our work, some investigators have performed maximal subtotal thyroidectomies, but the results have been disappointing, the metabolic rate has returned to normal, and the clinical condition has been unimproved.

Discussion of paper on "Theophyllin in the Treatment of Arteriosclerotic Heart Disease," by Drs. Smith, Paul, and Rathe.

Dr. Cooksey, Detroit, Mich.—Of interest in connection with Dr. Rathe's paper is an event which occurred in our cardiac clinic at Harper Hospital in Detroit. We have been faced with rigorous curtailment of the cost of drugs to patients of the Out-Patient Department. In treating angina of effort and related disturbances, we found it necessary to use something extremely inexpensive. A comparative study was made on a series of cases to determine whether theophyllin and all the closely related substances thereto were, after all, any more effective than some of the less expensive substances. The one to which we first, of course, turned, was the alkaloid of theobromine. As you probably know, it is very inexpensive.

We found that by the use of theobromine alkaloid, the effects in relieving angina pectoris and nocturnal dyspnea seemed just as good as they were in our private patients who were receiving metaphyllin and theocin. Also comparative studies were made on the same patients by the use of the various drugs with the same results. It has been our experience that theocin often produces nausea if given in very large amounts, so we do not often use it. Metaphyllin works extremely well.

Discussion of paper on "Tolerance to Digitalis in Patients With Normal Hearts and in Those With Arteriosclerotic Heart Disease," by Drs. McMillan, Bellet, and Robertson.

Dr. Samuel Bellet, Philadelphia, Pa.—The statement is often made that digitalis should be given until beneficial effects are obtained, or until the patient vomits. If this procedure is followed, many severe toxic reactions will occur.

In the normal group, 17 of our 20 patients vomited. They all received massive doses of the drug, and in spite of vomiting they showed no serious toxic effects.

In none of this group were extrasystoles, which we consider as definite evidence of toxicity, present even after the large doses administered. The group with slight myocardial disease reacted practically like the normal group. In the group with advanced myocardial disease only 9, or 40 per cent, of the patients, vomited. The remainder developed severe toxic reactions before vomiting occurred. These reactions, in 12 of this group, consisted of psychosis in two cases, severe visual disturbance in one, marked asthenia in three, and most important, the presence of toxic rhythms (ventricular tachycardia, complete A-V block, auricular tachycardia, nodal rhythm and bigeminal rhythm) in six patients. All these patients belonged to the arteriosclerotic group. In many of these patients, the toxic reactions were produced at comparatively small doses. We regard this point, namely that toxic digitalis manifestations may appear without the patient's vomiting, as extremely important. If this is kept in mind, many toxic reactions may be avoided.

In addition to the evidence which has been presented that a diminished tolerance to digitalis exists in patients with advanced heart disease, we should like to mention some evidence from the experimental standpoint. We took a series of normal dogs and standardized them with digitalis. We then produced cardiac damage in a series of these animals by tying the coronary arteries. These animals were standardized during the stage of acute, subacute, or chronic infarction. We found definitely diminished tolerance during the stages of subacute infarction, during which the infarcted area is at its maximum.

In conclusion, there are two points especially which we should like to make. First, patients with advanced myocardial disease exhibit a diminished tolerance to the digitalis as compared with a normal group. This diminished tolerance is, apparently, especially pronounced in the arteriosclerotic group. Second, toxic rhythms and other evidences of digitalis toxicity may be present without the patient's vomiting.

Department of Reviews and Abstracts

Selected Abstracts

Gordon, Wayne, and Adams, Wright: Estimation of Cardiac Transverse Diameter in Children and Comparison With Cardiac Area. Am. J. M. Sc. **188**: 491, 1934.

The relations of cardiac area and cardiac transverse diameter as measured by the roentgen ray, to sitting height, height, weight and age have been studied in a group of normal children. Both measures correlate better in children with weight than with height or age.

An equation is presented for the prediction of normal transverse diameter, and a comparison is made with cardiac area prediction formulas previously published from the same material.

Cardiac area in normal children can be predicted with greater accuracy than transverse diameter by any of the measures used. The advantage of cardiac area over transverse diameter as a measure of normal heart size appears to be greater in children than in adults.

Roesler, H.: Interatrial Septal Defect. Arch. Int. Med. **54**: 339, 1934.

A case is reported which illustrates the clinical and anatomic peculiarities of interatrial septal defects. Sixty-two cases have been reviewed. All of the cases of small defects or complete absence of the interatrial septum and combinations with patency of the ductus arteriosus, pulmonary stenosis, interventricular septal defect, and a high grade of coarctation of the aorta have been excluded.

In at least three-fourths of all the cases, valvular lesions were found which affected predominantly the mitral orifice. Subacute bacterial endocarditis did not occur; chronic pericardial disease, crossed embolism and tuberculosis of the lungs occurred rarely.

Almost all of these hearts were large; they were often of enormous size, even in the absence of a valvular lesion. This was entirely, or almost entirely, due to a right-sided enlargement, dilatation exceeding hypertrophy in a disproportionate degree. The left side underwent relatively little change from narrowness to a moderate increase in size. The average heart weight for nineteen patients above the age of fourteen years was 574 gm., and in nine cases of complete or almost complete absence of valvular lesions it was 469 gm. There was some evidence that the size of the heart was influenced by the size of the interatrial defect. The pulmonary artery was always larger than the aorta, the average ratio being 3:2. Expressed in absolute figures, the pulmonary artery was large or very large, but rarely normal in size. The aorta was usually below the normal figures, often being very small and thin walled. The branches of the pulmonary artery were often dilated, the artery as well as its branches being the seat of atherosclerotic processes. As seen in situ, the right side of the heart formed the entire front wall; the pulmonary conus extended far to the left and upward, and the aorta was placed between the pulmonary artery and the superior vena cava.

This cardiovascular malformation can be best conceived in its entity by assuming that there was added to the congenital arrest of development an acquired

hydraulic disturbance, a shunt from left to right, as a result of which the right side of the heart and the lesser circulation handled an increased amount of blood and the left side of the heart and the greater circulation a decreased amount of blood. The indirect evidences for this theory were given.

The average age was thirty-six years; the prognosis as to duration of life was about equal with that in coarctation of the aorta, less than that in the interventricular septal defect and better than that in patency of the ductus arteriosus and pulmonary stenosis. Repeated pregnancies, anesthesia, and capacity for physical work were well supported in a number of cases; in others, however, chronic invalidism was present. The common combination with chronic valvular lesions did not aggravate the prognosis. There was prevalence of the female over the male sex in the proportion of 3:2, similar to the ratio in patency of the ductus arteriosus.

The clinical course was that of ordinary cardiac failure, lasting for shorter or longer, periods, even when all the cases with valvular complications were omitted. Clubbing was sometimes present. Cyanosis was more often present than not, but the combination with lesions of the mitral and tricuspid valves is to be remembered. Pallor, a small radial pulse, and a tendency to a lower blood pressure were rather common. These findings may be understood as an expression of actual arterial underdevelopment and/or a decreased output of blood into the greater circulation. Other clinical findings were an expression of the enormous right-sided enlargement of the heart. These were: the precordial bulge; certain features of the apical thrust (circumscribed and resistant, indefinite and systolic retraction); systolic propulsions and depressions of smaller or larger parts of the thoracic wall (important for differential diagnosis from chronic pericardial disease); the occurrence of a systolic or presystolic pulse in the veins and liver, which was influenced by venous fullness, the presence of sinus rhythm or auricular fibrillation; and the occurrence of regurgitation of the tricuspid and mitral valves. Auricular fibrillation was common; in this the interatrial septal defect distinguished itself entirely from all other congenital cardiovascular malformations in which auricular fibrillation was of the greatest rarity. The same cause obviously was responsible for auricular fibrillation and chronic valvular deformity, especially of the mitral orifice. The common occurrence of an accentuation of the pulmonic second sound was mainly an expression of a concomitant lesion of the mitral valve. In the absence of this lesion accentuation was sometimes present. Murmurs were at times absent. When present, however, they were more commonly due to the combination of valvular lesions. In the absence of lesions, there was still dilatation of the pulmonary artery to be considered with or without changes in the wall and relative insufficiency of the orifice as the cause of murmurs which were probably thought to be characteristic of the defect. If a characteristic murmur of this sort existed, it was midsternal systolic, probably partly diastolic and not accompanied by a thrill.

The roentgenologic findings were those of a large heart varying in shape from oval to globular and extending, as a rule, toward the left. The pulmonary conus and artery projected far to the left and upward and forward. The branches of the pulmonary artery (the "hili") at times showed increased pulsations and were sharply defined and enlarged. Lack of knowledge of the roentgenologic picture led to the erroneous diagnosis of mediastinal tumor or tuberculosis. The aortic knob was small—at times invisible. Other conditions which caused pulmonary dilatation and narrowness or absence of the aortic knob were given.

The interesting finding from the electrocardiographic study was the presence, as a rule, of only a moderate degree of axis deviation to the right. Enormous dilatation of the right side of the heart with comparatively moderate hypertrophy did not cause a high degree of right axis deviation in the electrocardiogram.

Weiss, Soma, and Ferris, Eugene B., Jr.: Adams-Stokes Syndrome With Transient Complete Heart-Block of Vagovagal Reflex Origin. Arch. Int. Med. 54: 931, 1934.

This study centers around observations on a patient who for ten years suffered from attacks of fainting precipitated usually by the swallowing of food. The patient had a traction diverticulum of the esophagus, distention of which with the aid of a rubber balloon promptly induced auriculoventricular dissociation of the heart and syncope. The release of pressure in the balloon was associated with a prompt return of normal sinus rhythm and the disappearance of symptoms. The Adams-Stokes attack in this case was induced by heart-block precipitated by a vagovagal reflex. The source of the reflex was irritation of the sensory endings of the vagi by the diverticulum.

Various studies on blood flow and the effects of drugs on the attacks of heart-block are reported. The relative rôle of organic cardiac lesions and of neurogenic factors in the precipitation of Adams-Stokes attacks with heart-block is discussed and the simultaneous presence of multiple etiologic factors is stressed.

Weiss, Harry: Relation of Portals of Entry to Subacute Bacterial Endocarditis. Arch. Int. Med. 54: 710, 1934.

Results of a study of 364 cases of subacute bacterial endocarditis suggest that the common portal of entry of the streptococcus is from foci of infection in the passages of the upper respiratory tract and the mouth. Other portals of entry are the genitourinary tract, otitic infections, and wound infections. There is no evidence of the gastrointestinal tract as the portal of entry in any of the cases. The onset with an acute infection of the upper respiratory tract or tonsillitis in many cases led to the conclusion that in these apparently benign infections a transient bacteremia may occur. The frequency of antecedent cardiac disease, usually rheumatic but sometimes atherosclerotic or syphilitic, or some congenital lesion, indicated that the streptococcus probably requires a previously diseased or abnormal endocardium on which to implant itself.

Ten cases of subacute bacterial endocarditis are reported in which a history of tonsillectomy or extraction of a tooth closely antedated the onset of symptoms, indicating that trauma of an infective focus about the teeth and pharynx may produce transient bacteremia and thus play a part in promoting implantation on the endocardium.

Hamman, Louis: Sudden Death. Bull. Johns Hopkins Hosp. 55: 387, 1934.

Among the many causes of this phenomenon the author believes three are the most important. These are: sudden stopping of the heart, hemorrhage, and arterial embolism and thrombosis. Death due primarily to cardiac standstill occurs under two different circumstances: first, when the heart after a prolonged struggle against overwhelming difficulties finally plays out; second, when the heart while satisfactorily performing its work suddenly stops. Death due to the first cause can hardly be called sudden, since the overwhelming difficulties usually have been present sufficiently long to give warning of the impending end.

The author describes the second cause of sudden stopping of the heart as being due probably to ventricular fibrillation. He believes this condition occurs more frequently than is generally recognized and that many unexplained sudden deaths are due to this disturbance of mechanism. This probably is particularly true in those cases in which very little anatomical change can be found in the heart muscle at autopsy. Often only slight changes are found in the myocardium, small areas or scarring of a small infarct, and yet, these apparently trivial lesions may perhaps be enough to inaugurate the fatal rhythm.

Considerable space is given to the diagnosis of the causes of sudden death.

Fishberg, Arthur M., Hitzig, William M., and King, Frederick H.: Circulatory Dynamics in Myocardial Infarction. Arch. Int. Med. 54: 997, 1934.

Fifty-nine patients with recent myocardial infarction were studied from the point of view of circulatory dynamics. The venous pressure was measured in all, the circulation time in thirty-eight and the volume of circulating blood in twenty-nine of the subjects.

Two distinct mechanisms participate in the derangement of the circulation in myocardial infarction: (a) shock, or peripheral circulatory failure, which diminishes the venous return to the heart and tends to lower the pressure in the large systemic veins; and (b) heart failure, which tends to engorge the pulmonary circuit in consequence of insufficiency of the left side of the heart and to raise the systemic venous pressure in proportion to the insufficiency of the right side of the heart.

In initial myocardial infarction in persons without previous severe heart failure, the clinical picture is most often predominantly that of shock. The venous pressure is then subnormal. The blood flow through the lungs is slowed but little, if at all. The volume of circulating blood tends to be diminished.

When infarction affects patients with previous heart failure, the manifestations of either shock or cardiac insufficiency may be predominant. When heart failure dominates, the venous pressure is elevated or normal, the flow of blood through the lungs is retarded, and the volume of circulating blood is increased.

The diminished venous return due to shock lessens the work of the heart and thus militates against the development of cardiac insufficiency. It is because of this diminution in the venous return to the heart that engorgement of the lungs and systemic veins may be absent despite extensive myocardial infarction.

The fall in arterial pressure is due not only to the weakness of the left ventricle but also to the peripheral circulatory failure of shock. Apparently the latter is usually the more important of the two factors. It is because of the concomitant presence of shock that a fall in the arterial pressure is so much more prominent in myocardial infarction than in other lesions of the heart.

Statistically, the immediate prognosis of myocardial infarction is better with low than with high venous pressure.

The type of circulatory failure present is of significance for the rational treatment of patients with myocardial infarction.

Wayne, E. J., and Graybiel, Ashton: Observations on the Effect of Food, Gastric Distention, External Temperature, and Repeated Exercise on Angina of Effort, With a Note on Angina Sine Dolore. Clin. Sc. 1: 287, 1934.

An average reduction of 25 per cent in exercise tolerance occurred after a heavy meal in six patients with pure angina of effort. In the same six patients, exercise tolerance was unaffected by inflation of the stomach with air, even when sufficient was introduced to give epigastric discomfort and to displace the heart. It is concluded that in angina of effort the reduction of exercise tolerance after food is due to the increased energy expenditure of the heart and not to gastric distention. In normal individuals large amounts of air were introduced into and retained by the stomach. While the stomach was distending, slight changes in pulse and blood pressures occurred, but, when the stomach had adapted itself, no changes in the cardiovascular system could be detected even though the heart was mechanically displaced.

A case of spontaneous angina is described in which both food and gastric inflation gave rise to attacks; it is considered likely that distention of the stomach can reflexly initiate an attack of this type of case.

Variations in the external temperature did not affect exercise tolerance in six patients with angina of effort. Two types of angina of effort exist; in both, exercise tolerance is constant if sufficient rest is allowed between the end of one attack and the start of the next test. In one type, as this period of rest is reduced, exercise tolerance gradually diminishes; in the other, there is a phase which may be as long as an hour, during which exercise tolerance is increased. Diminishing the rate of exercise had no effect in two patients, and in four gave a moderate increase in the total amount of exercise performed.

A case is described in which the symptoms resembled those previously described under the term "angina sine dolore." Investigation showed that the attacks were due to paroxysmal ventricular action brought on only by exercise. The conception of "angina sine dolore" is briefly discussed.

Poynton, F. J.: Some Aspects of Heart Disease in Childhood. Bristol Med.-Chir. J. **51**: 205, 1934.

In this Long Fox Memorial Lecture, the author describes the various forms of heart disease occurring in children, including tuberculous and meningococcal heart disease. He reviews his own previous work and ideas developed a good many years ago and correlates them with the findings of heart disease at the present time. He particularly emphasizes the importance of apyrexial carditis and states that this form is repeatedly seen in children under the age of five years. In his own study he has found the incidence to be about 10 per cent. He also states that the mortality at this age is proportionately greater than at any period.

He discusses particularly the etiology of heart disease at this time of life and points out the difficulty in correlating the finding of rheumatic carditis with malignant endocarditis.

Pickering, G. W., and Wayne, E. J.: Observations on Angina Pectoris and Intermittent Claudication in Anemia. Clin. Sc. **1**: 305, 1934.

Pains clinically indistinguishable from those of intermittent claudication and angina pectoris may occur in any type of severe anemia. Of twenty-five consecutive ambulatory cases of severe anemia, seven complained of pain in the legs and eight of pain in the chest induced only by exercise and relieved by rest. After cure of the anemia only one patient experienced pain in the legs and two pain in the chest. In nine patients grossly anemic, exercise of the limbs without circulatory arrest produced severe pain having the characteristics of intermittent claudication. After cure of the anemia similar exercise produced no or only slight pain. After a given amount of exercise, blood flow through the active muscles is at least as great in the anemic as in the nonanemic state. It is suggested that the stimulus which produces the pain of intermittent claudication is an accumulation in the tissue spaces of metabolites normally removed by oxidation.

In six severely anemic patients, complaining of sternal pain or tightness on walking, the sensation was reproduced by exercise tests. In four patients, the same exercises no longer produced pain or tightness when the blood contained more than 50 per cent of hemoglobin. In two patients, the exercise tolerance increased with rising hemoglobin content of the blood, but pain could still be induced when the blood was normal. The reaction of heart rate and blood pressure to exercise is usually altered in anemia, and such alterations may contribute to the development of anginal pain. It is concluded, however, that the essential factor in the production of anginal pain is a diminished oxygen supply to the working heart muscle.

These observations support the view that angina pectoris and intermittent claudication are due to similar mechanisms operating in the heart and skeletal muscles. Reasons are given why some, but not all, anemic patients complain of angina or of intermittent claudication.

No electrocardiographic changes characteristic of myocardial anoxemia were detected in anemic patients after exercise. In two patients the P-R interval was abnormally long in the anemic state and was within normal limits after cure of the anemia.

Berlin, David D., Blumgart, H. L., Weinstein, A. A., Riseman, J. E. F., and Davis, David: Treatment of Angina Pectoris and Congestive Failure by Total Ablation of the Normal Thyroid Gland. New England J. Med. **211:** 863, 1934.

The present report deals with three surgical problems in the technic of the operation for total ablation of the thyroid gland. The value of the various anesthetics is also discussed. In seventy-five operations, there have been three permanent unilateral nerve injuries. No severe manifestations of parathyroid insufficiency have occurred in this group. Two patients still require calcium therapy, but their symptoms are completely controlled. By modification in pre- and postoperative treatment, improvement in surgical technic and by the use of local anesthesia, the last thirty-six consecutive patients with chronic heart disease have been operated on without mortality.

The results of total thyroidectomy for the treatment of chronic rheumatic heart disease are reported and compared with those obtained in the treatment of arteriosclerotic heart disease. Twenty-nine patients have been treated by total thyroidectomy. Of these, twenty-five had congestive failure, three had congestive failure and angina pectoris, one had angina induced by paroxysmal auricular fibrillation, and one had congestive failure and rapid heart action.

The incidence of good results was somewhat greater in these patients with rheumatic heart disease than in those with arteriosclerotic heart disease. Although it is difficult to be certain of all the factors which account for the differences of two such dissimilar groups of patients, certain considerations are worthy of mention. The preoperative basal metabolic rate is more likely to be normal or higher in the rheumatic group than in the arteriosclerotic group, and it has been shown that the higher the metabolic rate, the greater will be the relief following total thyroidectomy. Also a history of previous coronary thrombosis will limit the satisfactory results following thyroidectomy. Since coronary thrombosis is rare in rheumatic heart disease, this factor will seldom require consideration in such patients. The patients with arteriosclerotic heart disease were definitely older, and these patients are more subject to cerebral hemorrhage or thrombosis as well as coronary thrombosis, and for this reason the ultimate results are not so satisfactory as the results in the group of rheumatic heart disease which was definitely younger.

Cassio, P., and Berconsky, I.: Non-apparent Cardiac Insufficiency. Rev. Argentina de Cardiologia **1:** 11, 1934.

An analysis of the blood, respiratory and circulatory functions in twenty-seven patients with diverse cardiovascular disturbances but showing none of the symptoms of cardiac insufficiency (dyspnea, visceral congestion, etc.) showed that about 80 per cent of these patients had a decreased efficiency of the heart as a pump. The authors suggest the name of nonapparent (inapparent) cardiac insufficiency to designate this condition, to indicate that the cardiac insufficiency is not easily recognized by the ordinary methods of examination.

The authors believe that these patients may have a diminished efficiency of the heart in spite of the absence of either respiratory or visceral congestion

and show this by an increased heart rate, a lowered pulse pressure, and especially definite enlargement of the heart. These findings should indicate a structural alteration of the cardiovascular system. If a lowered velocity of blood flow, an increased difference in the venous and arterial oxygen content, and decreased vital capacity, etc., are found, this diagnosis will be confirmed.

The authors conclude from their study that digitalis should be prescribed for these patients suffering from nonapparent cardiac insufficiency in order to delay the possibility of its becoming an apparent one.

Page, Irvine H., and Heuer, George J.: A Surgical Treatment of Essential Hypertension. J. Clin. Investigation **14**: 22, 1935.

Section of the anterior nerve roots from the sixth thoracic to the second lumbar segment has been performed in a young girl suffering from persistently elevated arterial blood pressure. Anatomical and physiological evidence indicated that her vascular system was yet flexible.

The blood pressure level quickly fell to normal and has remained normal for seven months.

Denervation of the kidneys resulting from the operation did not alter their power to excrete urea, but there was slight loss in ability to concentrate urine. The kidneys were as efficient when the blood pressure was reduced to normal as when it had been elevated. No increase occurred in the number of red blood cells excreted in the urine.

In spite of the fact that the blood pressure fell to normal, there was no change in the subjective feeling of the patient except that headaches, palpitation, and the precordial pain disappeared.

No significant alterations occurred in the hemoglobin and plasma proteins. The basal metabolism and cardiac output also were normal. Electrocardiographic records taken before and after operation showed no change from normal.

Determinations were made of total lipid, total and free cholesterol, lipid amino nitrogen, total lipid nitrogen, and lipid phosphorus in the blood plasma both before operation, when the blood pressure was elevated, and after, when it was normal. Except for slight rise in lipid amino nitrogen and total lipid nitrogen following operation, the changes were insignificant.

Page, Irvine H., and Heuer, George J.: The Effect of Renal Denervation on the Level of Arterial Blood Pressure and Renal Function in Essential Hypertension. J. Clin. Investigation **14**: 27, 1935.

Bilateral renal denervation in a patient suffering from severe essential hypertension did not change the level of arterial blood pressure; hence the results give no ground for expecting that denervation in cases of essential hypertension is of therapeutic value. No ill effects either renal or extrarenal were observed after denervation. Renal efficiency as measured by the urea clearance test and the ability of the kidneys to concentrate was normal before operation and remained unchanged after denervation. The results do not support the hypothesis that essential hypertension originates in whole or in part in the nervous mechanism of the kidneys.

Friedlander, Richard D., and Levine, Samuel A.: Auricular Fibrillation and Flutter Without Evidence of Organic Heart Disease. New England J. Med. **211**: 624, 1934.

An analysis has been made of thirty-five cases of auricular fibrillation and four cases of auricular flutter in which no other signs of cardiac disease were demonstrable and in which rheumatic heart disease, coronary artery disease, hy-

pertension, hyperthyroidism and syphilis could not be considered contributory. These cases composed approximately 6 per cent of all patients with auricular fibrillation and 20 per cent of all those seen with auricular flutter during the same number of years in private practice.

Of the thirty-five cases of auricular fibrillation, thirteen were classified as transient and twenty-two as permanent. Less than half of the patients in the entire group were over fifty years of age, and there were only three females in all.

In those cases with transient auricular fibrillation, the average at the onset was thirty-two years for those under fifty years of age and fifty-two years for those over fifty years of age. In the patients with permanent auricular fibrillation, the averages were forty-seven years and fifty years for the two age groups.

The blood pressure, basal metabolism, vital capacity, and laboratory findings were considered to be within normal range for the entire series. Cardiac examinations were entirely negative in all. Roentgenograms were obtained in one of the transient cases and in nine of the permanent group and, except for very slight cardiac enlargement in one case in each group, were considered negative.

The inciting factor was elicited in nine of the patients with transient fibrillation and somewhat less definitely in six of those in the permanent group. Included in these incitants in the order of frequency were exertion, gastrointestinal disturbances, alcohol, and upper respiratory infections.

Experiences with treatment in this small group of cases would seem to indicate that digitalis may diminish the frequency of transient attacks of fibrillation, but is practically ineffective in restoring normal rhythm in the permanent group. Quinidine is generally effective in establishing a normal rhythm in this latter group.

All the patients with auricular flutter were males, three of whom were over sixty years of age, the other was thirty-eight years old. Cardiac examinations were negative in all. Pneumonia in one patient and exertion in two of the others were the only possible inciting factors. No conclusions can be drawn regarding the effect of medication in this small group of cases, except that digitalis restored the rhythm to normal in two of the patients and quinidine in another.

The assumption has been made that in such cases as these under discussion, the mode of onset of the irregularity may be the result of a "trigger" mechanism of neurogenic origin in certain otherwise normal individuals with hyperreactive or unstable nervous systems. This mechanism may be related to that associated with the onset of similar arrhythmias in hyperthyroidism.

This study emphasizes the fact that auricular fibrillation and flutter must be regarded in some cases as benign or functional arrhythmias.

Thomson, William A. R.: The Plasma Proteins and Cardiac Edema. Quart. J. Med. 3: 587, 1934.

The results are recorded of an investigation of the plasma proteins in fifty-four patients, consisting of eighteen cases of heart failure with edema, sixteen cases of heart disease accompanied by edema, six cases of Bright's disease, four cases of tuberculosis, a miscellaneous group of seven cases and three junior members of the hospital staff who were used as normals. In all, eighty-seven estimations were made.

There is a distinct diminution in the plasma proteins in cardiac edema, 87.5 per cent of the cases having a plasma albumin content of less than 3.2 gm. per cent. In heart disease without edema, there is only a slight diminution in the plasma proteins as compared with the normal, 87 per cent of the patients having a plasma albumin level greater than 3.2 gm. per cent.

In view of these findings it is suggested that plasma protein deficiency plays an important rôle in the etiology of cardiac edema. The main cause for the plasma protein depletion in cardiac edema is considered to be malnutrition. It is suggested that the dietary of patients with cardiac edema should contain the maximum amount of protein compatible with their digestive powers.

Lewis, Thomas, and Pickering, G. W.: Observations Upon Maladies in Which the Blood Supply to Digits Ceases Intermittently or Permanently and Upon Bilateral Gangrene of Digits; Observations Relevant to So-Called "Raynaud's Disease." Clin. Sc. 1: 327, 1934.

The purpose of the paper is to show that a number of distinct conditions have been described under the term "Raynaud's disease," separately to explore these, and to indicate directions in which new inquiries may be conducted. It is considered that the term "Raynaud's disease" should be abandoned.

The present inquiries again point to the existence of a local fault as a cause of both Raynaud's disease and of bilateral gangrene. The several causes of local faults of the vessels are enumerated:

Intermittent spasm of digital arteries with generalized scleroderma.

Raynaud's phenomenon arising out of local injury, including the use of vibrating tools.

Bilateral gangrene of digits in the young, and with infection; this condition is regarded as probably the result of thrombotic closure of vessels.

Bilateral gangrene with hemoglobinuria from cold, a condition having probably a unique pathogeny.

Bilateral gangrene of digits in the elderly, in which closure is shown to be thrombotic but preceded by disease of the small arteries.

Thromboangitis obliterans associated with Raynaud's phenomenon.

Cervical rib or crutch pressure causing Raynaud's phenomenon or gangrene, so it is thought, by thrombotic and embolic processes.

It is suggested that gangrene is never the result of uncomplicated spasm of arteries. Evidence tends increasingly to show that gangrene depends upon structural occlusion of the vessels.

Pickering, G. W.: The Cerebrospinal Fluid Pressure in Arterial Hypertension. Clin. Sc. 1: 397, 1934.

The general clinical features presented by hypertensive patients with cerebrospinal fluid pressures of 250 mm. water and over contrast strongly with those presented by patients having lower pressures. The former are younger, the kidneys are usually severely damaged, and the disease progresses rapidly to a fatal termination. The latter are older, the kidneys usually escape severe damage, and the disease progresses less rapidly.

Every patient with a cerebrospinal fluid pressure over 250 mm. water developed albuminuric retinitis. With one exception, every patient with a lower cerebrospinal fluid pressure had either no retinal lesion or the lesions characterizing arteriosclerotic retinitis. It is suggested that the essential difference between these two forms of retinitis is the addition in the albuminuric type of neuroretinal edema resulting from increased intracranial pressure.

In individual patients with high blood pressure, the cerebrospinal fluid pressure has been found unaltered during headache and during acute attacks of coma and convulsions unassociated with uremia.

There is a relation between high diastolic blood pressure and high cerebrospinal fluid pressure, and it is suggested that the former is one of the factors determining the latter.

Book Reviews

DAS BERIBERI-HERZ: MORPHOLOGIE, KLINIK, PATHOGENESE. By Professor K. F. Wenckebach, in charge of the First Medical University Clinic in Vienna. Julius Springer, Berlin and Vienna, 1934, 106 pages, with 38 illustrations.

Professor Wenckebach's monograph on the beriberi heart is the outcome of an invitation visit to Java; and the book reflects his great interest in this problem, as well as in other types of heart disease, and the friendly cooperation of the men with whom he worked. Even in our own part of the world where beriberi, far from being an important public health problem, is a rarity, the study should be read with great interest. "Shôshin," the rapidly fatal affection of the heart which appears in some cases of beriberi, presents a striking clinical picture—the picture of a rapidly developing and extreme degree of pure right-sided failure unassociated with valvular damage or with evidences of failure of the left ventricle. The patient is seen complaining of severe epigastric and retrosternal pain, writhing and tossing in bed, equally distressed whether erect or reclining, breathing rapidly and superficially; the veins and liver are tremendously enlarged and pulsating, and the lungs are free from any sign of congestion. After focussing the reader's attention on the clinical picture of shôshin Professor Wenckebach presents the gross and microscopic anatomy, the characteristic x-ray picture, and the heart of infants affected with beriberi. He then describes some of the physical signs in greater detail, stressing particularly the enormous enlargement of the heart, the peripheral vascular signs, and the remarkable response to certain hormones. There is a prompt exacerbation of all symptoms upon the injection of adrenalin and an equally prompt improvement following the injection of pitressin; the results of which are so dramatic that the former drug is used as a diagnostic aid to measure improvement during convalescence, and the latter is considered as of possible therapeutic value. In the final section of the study the author takes up certain theoretical considerations—the nature of the water retention, which differs from edema, the relation between muscle tonicity and contractility, the disproportion between the involvement of the right and left sides of the heart, the basis underlying the vascular signs, the part played by the glands of internal secretion, the relation between the nervous manifestations and the disturbance of the skeletal and cardiac muscles. These are fundamental problems, of great interest and importance whether or not we ever see a case of beriberi heart.

E. H.

ENFERMEDADES DEL PERICARDIO. By Dr. Carlos P. Waldorp and Dr. Samuel Genijovich. Aniceto Lopez, Buenos Aires, 1934.

This volume of more than four hundred pages represents a praiseworthy attempt to cover the entire field of diseases of the pericardium. The book is systematically arranged and freely illustrated. Most of the subjects are covered adequately.

The extensive bibliography loses some of its value because neither the volume nor the page is given in the references.

The book should find a distinct field of usefulness in Spanish-speaking countries.

L. A. C.

PHYSIOLOGY IN HEALTH AND DISEASE. By Carl J. Wiggers, M.D., Professor of Physiology in the School of Medicine of Western Reserve University, Cleveland, Ohio. Lea & Febiger, Philadelphia, 1,184 pages, with 182 illustrations.

To all those familiar with Dr. Wiggers' classic monograph, *The Circulation in Health and Disease*, the plan and character of the new volume will at once be apparent. He has extended to the whole field of human physiology the method employed in his earlier book on the circulation.

It is obvious that the plan of presenting side by side the normal and the pathological aspects of physiology has many and great advantages to every one—student, general practitioner, and clinician—whose interest in physiology lies primarily in its application to the problems of clinical medicine.

In this treatise of some 1,200 pages, almost 300 pages are devoted to the section on "Heart and Circulation." This portion of the new book follows the general lines of the author's earlier one, although the section has been entirely rewritten and extensively revised. The text of this section has been condensed to about one-half that of the earlier book; but in spite of this, much important new material has been added. The recent advances concerning the peripheral blood vessels are fully recorded, and there is a new and admirable chapter on the coronary circulation and its disturbances. Indeed, throughout the entire volume there is constant evidence of the effort to bring the whole field of physiological knowledge into relationship with the everyday problems of clinical medicine.

The appearance of Dr. Wiggers' book is an event of the first importance to every one interested in tightening the bonds between physiology and the clinical sciences.

L. A. C.

THE HEART VISIBLE. A CLINICAL STUDY IN CARDIOVASCULAR ROENTGENOLOGY IN HEALTH AND DISEASE. By Dr. J. Polevski, Attending Physician and Cardiologist, Newark Beth Israel Hospital. F. A. Davis Company, Philadelphia, 1934, 207 pages, with 122 illustrations.

In the preface Dr. Polevski states that this book is intended for the radiologist who has the scientific curiosity of a clinician and also for the cardiologist and for every clinician eager for any and every possible means that will enable him to establish a diagnosis that will be in keeping with the facts. He might also add that the book would be suitable for the medical student who is interested in learning the first principles of the fluoroscopic examination of the heart and great vessels. The text is simply written and generously illustrated, and the illustrations have been carefully selected and well printed so that they really illustrate. The author stresses the value of careful observation, not only in the anteroposterior position, but also in the oblique and lateral positions, and one might wish that he had chosen to show more of the oblique views of the chest, particularly in relation to the study of the aorta and the distinction between dilatation and tortuosity. The work is useful in calling attention to a method of investigation which has not been sufficiently utilized, in illustrating the appearance of the cardiac silhouette under normal and abnormal conditions, and in discussing various extrinsic factors which if not properly interpreted may lead to mistakes in diagnosis. It probably contains little that is not familiar to the radiologist and the cardiologist for whom it was intended.

E. H.